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### OLIGURIA AND ANURIA IN TOXEMIAS OF PREGNANCY\*

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**D**EPRESSION of renal secretion constitutes one of the gravest complications of pregnancy. Although it may be due to a variety of pathologic lesions, this discussion will be limited to the syndrome of decreased renal output associated with the various types of toxemia. We will present and discuss nine cases which have come to our attention during the past five years, with the hope of emphasizing the importance of this disorder and its proper management.

A variety of terms have been utilized to describe the degree of renal suppression. According to Dieckmann,<sup>1</sup> anuria is defined as the total absence of any urinary secretion for a period of twelve hours or longer. Oliguria means a urinary output of 600 c.c. per twenty-four hours or less in the presence of an adequate intake and no other source of fluid loss. Other evidence of renal deficiency may be manifested by hematuria, proteinuria, abnormal formed elements in the urine, and general metabolic disturbances.

#### Incidence

The over-all importance of any problem is related to the frequency of its occurrence and its seriousness. Just how often renal suppression associated with toxemia occurs cannot be determined from the literature.

\*Read at the Tenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Augusta, Ga., Feb. 12 to 14, 1948.

NOTE: The Editors accept no responsibility for views and statements of authors as published in their "Original Communications."

TABLE I. INCIDENCE

Deliveries, North Carolina Baptist Hospital, January, 1943 to January, 1948	5,180
Cases of toxemia, North Carolina Baptist Hospital, 1943 to 1948	142
Cases of renal suppression, North Carolina Baptist Hospital, 1943 to 1948	7
University of Virginia (Dr. Norman Thornton)	1
High Point Memorial (Dr. Thomas Tyson)	1
Total cases of renal suppression	9

From Jan. 1, 1943, to Jan. 1, 1948, there were a total of 5,180 deliveries in the North Carolina Baptist Hospital. Among these, there were 142 cases diagnosed as toxemia of pregnancy; and, in this group, seven exhibited renal suppression. Of the seven patients, two had relatively mild forms of toxemia with premature separation of the placenta. The remaining five exhibited severe forms of toxemia. *Comment:* These figures should not be considered of statistical value since the shortage of personnel during the war years made accurate cross indexing impossible. No attempt has been made to group the toxemias according to the American Committee of Maternal Welfare classification<sup>2</sup> since many records did not contain sufficient information.

We have reason, however, to believe the incidence is much greater than is suspected. For instance, when this paper was in preparation, three cases from other hospitals came to our attention; two of which are referred to in this article. The other will be reported later by the attending physician. Three other cases which occurred in Winston-Salem were likewise brought to our attention.

### Etiology

The etiology of this syndrome is as yet obscure although certain encouraging leads have been discovered. Lucke<sup>3</sup> recently studied a series of 538 fatal cases from a clinicopathologic viewpoint. He concludes that a wide variety of etiologic agents produce similar renal lesions and that "it is appropriate to designate all cases exhibiting these renal disturbances, no matter what their etiologic background, by a single term." He designates the pathologic picture as "lower nephron nephrosis." Among the various causes of this renal lesion, he includes the following:

We are particularly interested in the last four etiologic agents.

TABLE II. ETIOLOGY

1. Crush syndrome
2. Thermal burns
3. Heat stroke
4. Blackwater fever
5. Chemical poisoning or sensitivity
6. Alkalosis
7. Hemolytic transfusion reactions
8. Nontraumatic muscular ischemia
9. Toxemia of pregnancy
10. Uteroplacental damage

### Pathology

The pathologic picture of lower nephron nephrosis depends upon the duration of the process as well as the severity of the original insult. Grossly, the kidneys are pale and swollen and the capsule strips readily. The cortex is considerably widened and pale in contrast to the medulla which is a dusky



red. Microscopically, there is a varying degree of necrosis of the lower nephron with relatively slight damage to the other renal structures. The interstitial tissue is edematous and shows moderate cellular infiltration. Examination of the tubules reveals a number of heme casts present. There may be evidence of vascular thrombosis in some areas of the kidney. The glomerular vessels are singularly free of red cells. Little or no pathology is found elsewhere in the body.

### Pathogenesis

The pathogenesis of this disorder is not completely understood. Many explanations have been offered but none have been accepted unequivocally. Very extensive studies on the crush syndrome during the war, however, have elucidated many of the features of the process. The present concept is that cellular destruction by one of the etiologic agents indicated in Table II releases a group of chemicals into the blood stream which, under the proper conditions, causes renal damage. So far, the following chemical substances have produced injury to the renal tissue in experimental animals.

TABLE III. CHEMICAL SUBSTANCES POTENTIALLY TOXIC TO KIDNEY

1.	Hemoglobin
2.	Myoglobin
3.	Hematin
4.	Methemalbumin
5.	Sulfhemoglobin
6.	Metmyoglobin
7.	Trypsin
8.	Adenosine triphosphate
9.	Creatine
10.	Potassium
11.	Uric acid

It is probable that two organs are primarily involved: the liver and the kidney. In the absence of secondary factors, the toxic products are handled without difficulty by the liver and kidney. Normally, the liver removes or detoxifies these chemicals with the excretion of harmless products or the reutilization of certain other products. In the case of the kidney, there is an increased concentration of these products which, in the absence of secondary factors, are excreted without suppression of urinary output.

In the abnormal state, however, the process varies in that some liver damage is present which leads to the failure of removal and detoxification of the products, and their concentration is increased in the blood stream. This leads to an abnormal concentration of these chemicals in the kidney. At this point, the secondary factors, such as decreased blood flow from vasoconstriction or reduced blood volume and acidosis, enter the picture. This combination leads to vasoconstriction and further reduction of the blood flow due to direct action of the chemical substances. In addition, there is actual chemical injury to the tubular cells. These factors acting together cause necrosis of the lower tubular cells. The selective resorptive power of the tubular cells, which maintain the proper balance of water and electrolytes in the body, is now lost. As a consequence of this inability, the larger molecules of the products of tissue destruction become concentrated and precipitate. These precipitated substances then cause further injury to the tubular cells. The diminution of urine, as stated by Bywaters and Dible,<sup>4</sup> "is now due to excessive but unselective reabsorption of the glomerular filtrate through the tubules—in other words, leakage back into the blood stream."

In the cases of transfusion reaction, crush syndrome, and premature separation of the placenta, the source of the injurious material is readily explained. However, in toxemias, uncomplicated by premature separation, the noxious agent is more difficult to discover. One might postulate that toxemia is complicated by tissue destruction, as evidenced by elevated uric acid levels.<sup>5</sup> The diagram below is a simple illustration of the probable pathogenesis of lower nephron nephrosis (Fig. 1).

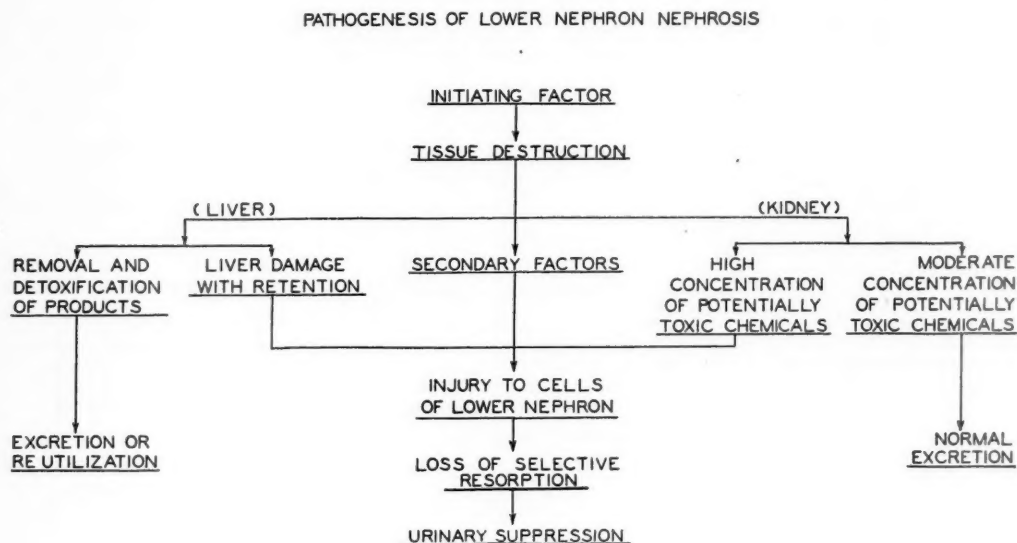


Fig. 1.

### Case Reports

With these preliminary remarks, we would like to present the following cases.

**CASE 1.** Mrs. M. C. P., NCBH No. 47786. A 42-year-old, married, white, gravida vi, para iv, abortus i, was admitted to the North Carolina Baptist Hospital on Jan. 13, 1946. Her calculated date of confinement was March, 1946. The patient had received no prenatal care. Five hours prior to admission, she began to bleed moderately from the vagina and to have pain over the entire abdomen.

Examination on admission showed her temperature to be 98° F., pulse 100, respiration 24, and blood pressure 120/90. The patient was a middle-aged woman who appeared anemic and in acute distress. The uterus was approximately four fingerbreadths above the umbilicus, quite firm and tender, and did not relax. No fetal heartbeat was present. She had a one plus pitting edema of the ankles.

She was immediately cross matched, and a sterile pelvic examination revealed the cervix to be 2 cm. dilated. No placenta could be palpated, and a breech presentation was noted. Membranes were ruptured and the patient received 500 c.c. of whole blood without reaction. At the time of pelvic examination, she was catheterized and 100 c.c. of clear, yellow urine were obtained with the specific gravity of 1.017, no albumin or sugar. Microscopic examination showed 2 to 4 white blood cells, 1 to 3 red blood cells, and no casts. Her hemoglobin was 11.5 Gm. with 4.32 million red blood cells.

Seven hours after the membranes were ruptured, the patient spontaneously delivered a 3 pound, 14 ounce stillborn male infant. The third stage was uncomplicated. She was

catheterized at the time of delivery and only 5 c.c. of dark, bloody urine were obtained. This urine had a two plus albumin and innumerable red blood cells with no casts or hematin crystals. The patient's blood pressure remained around 150/100. Eight hours after delivery this dropped to 100/70 but, two hours later, was fairly well established at 120/80.

Seven hours after the delivery, only 5 c.c. of a dark brownish urine was obtained. The patient had received a total of 4,000 c.c. of fluids intravenously since admission. During the next 18 hours, no urine was obtained. At 10 P.M. on Jan. 14, 5 c.c. of urine which was grossly bloody were obtained. The patient developed generalized edema but repeated examinations of her lungs revealed them to be clear. The patient was digitalized and received 2,000 to 3,000 c.c. of fluids daily, 500 of which consisted of 1/6 per cent molar lactate.

On January 15, her urine was still scanty, with a total of only 12 c.c. since the time of her delivery. A diagnosis of bilateral cortical necrosis of the kidney was made and a segmental block of sympathetic innervation with spinal anesthesia was carried out but failed to benefit the patient. Following this, the right kidney was decapsulated and a biopsy of the kidney was taken.

The pathologic diagnosis on the biopsy of the kidney was cortical necrosis. The microscopic description is as follows: marked necrosis of the tubules, most marked in the convoluted area. Cell outline remains in some instances, but the epithelium has been reduced to a pinkish granular substance. Interesting changes are also taking place in the capillaries in the form of pinkish, acellular deposits.

On the following day, 78 c.c. of urine was passed. The amount of fluid the patient received daily as well as other pertinent information can be seen in Fig. 2. It is interesting to note that on January 19 the patient received the smallest amount of fluids of her entire course and yet the following day her output reached the highest point it ever attained.

The patient's general condition remained fairly good until January 17, when vomiting began and moist râles were noted at the base of both lungs. She became irrational and on January 19 she was placed in an oxygen tent. From that time on until her death, January 25, her course was downhill with the nonprotein-nitrogen climbing. On the day of her death, moist râles could be heard throughout both lung fields and the patient was expectorating a frothy bloody fluid.

Autopsy performed shortly after death revealed the serous cavities to contain moderate amounts of reddish-yellow fluid. Each kidney weighed 175 Gm., the capsule of the left kidney stripped with ease, revealing an external surface slightly lobulated and of a pale reddish-brown color. Scattered petechial hemorrhages were seen on the surface. On sectioning, the cut surface bulged, the cortex was light, grayish-red containing numerous minute yellow streaks. The usual architecture was noted, and the pyramids were well formed. The capsule of the right kidney had been stripped and the surface in its gross appearance was similar to that of the left.

On microscopic examination, the most striking change was thickening and hyalinization as well as loss of cellular detail of the ascending arteriole at the point of entrance into the glomerulus. There is dilatation of some of the proximal convoluted tubules, a few of which are filled with an eosinophilic, homogeneous acellular material. A minimal necrosis is seen in a few of these tubules. The interstitial tissue of the entire organ appears slightly edematous. There was definite evidence of repair, compared to the picture seen at biopsy.

The remainder of the autopsy revealed only the terminal changes one would expect under the circumstances.

This patient exhibited a fairly typical clinical picture of advanced lower nephron nephrosis following premature separation of the placenta and toxemia. This was confirmed by biopsy of the kidney. Her renal output improved temporarily following renal decapsulation; but, as noted in the chart, her intake was not restricted and the patient died in congestive heart failure. We believe that, if fluids had been restricted, this patient

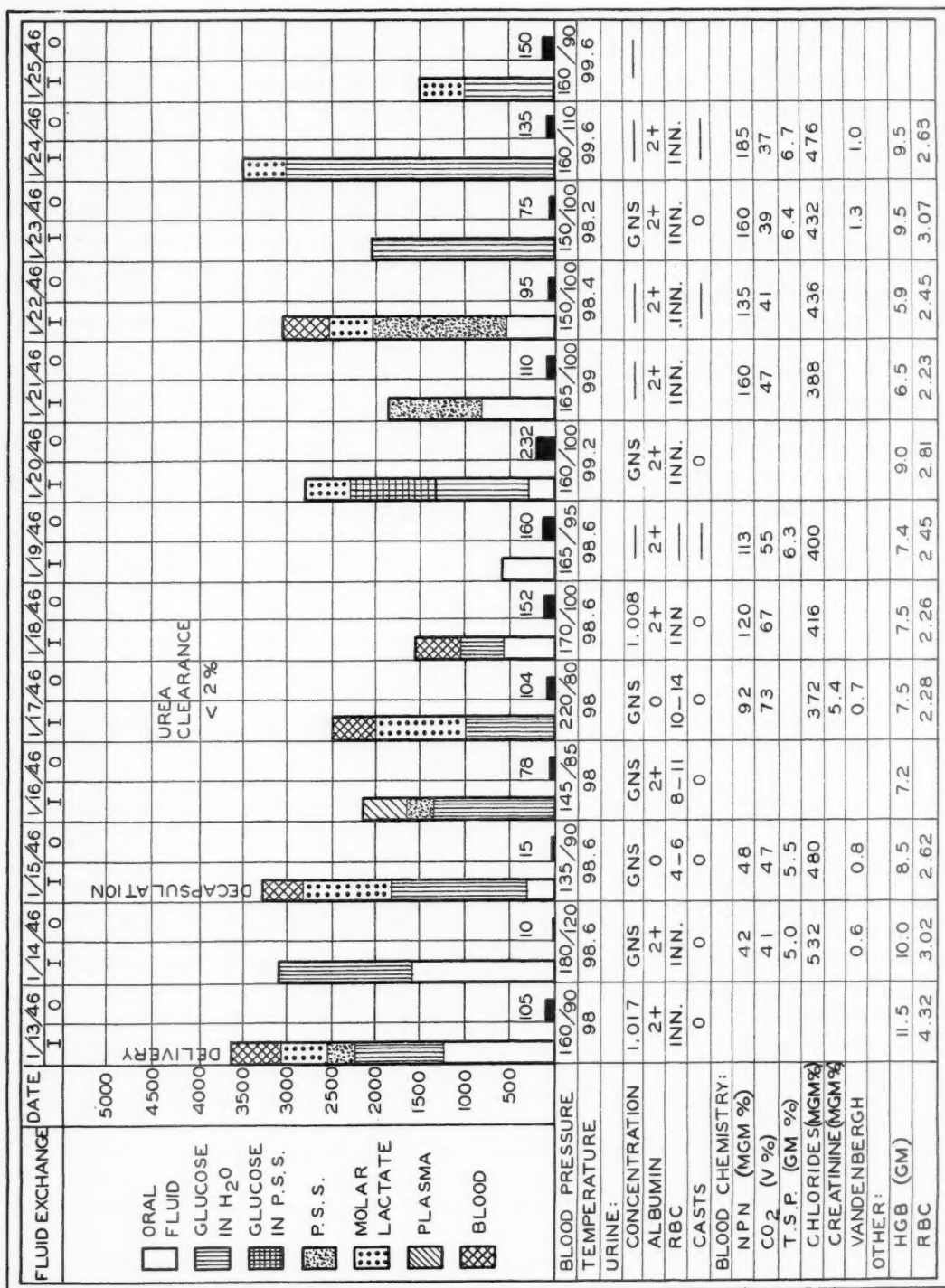


Fig. 2.—Case 1.



might have survived, and certainly her chances would have been greatly improved if peritoneal irrigation had been available. This case also demonstrates the ability of the kidney to regenerate, as shown at the autopsy.

In contrast to this case, we would like to present a case which has been given to us by Dr. Norman Thornton, of the University of Virginia Medical School.

CASE 2.—University of Virginia Hospital No. 233467. This 36-year-old, gravida vii, para iii, abortus iii, was admitted to the University of Virginia Hospital Nov. 28, 1946. Her expected date of confinement was March 2, 1947.

On admission, she was in profound shock with a blood pressure of 80/50. Examination of the abdomen at that time revealed a uterus slightly larger than a six months' gestation. The uterus was hard and tender, some vaginal bleeding was present. Sterile pelvic examination revealed the cervix to be long and closed. The patient received a 1,000 c.c. of whole blood and had a mild reaction with the second 500 c.c. At the time of admission, her hemoglobin was 7.5 Gm. and her red count was 1.8 million. The patient was Rh positive and Type A. She subsequently received a total of six transfusions. All transfusions were Type A and compatibility tests were done on each bottle of blood given.

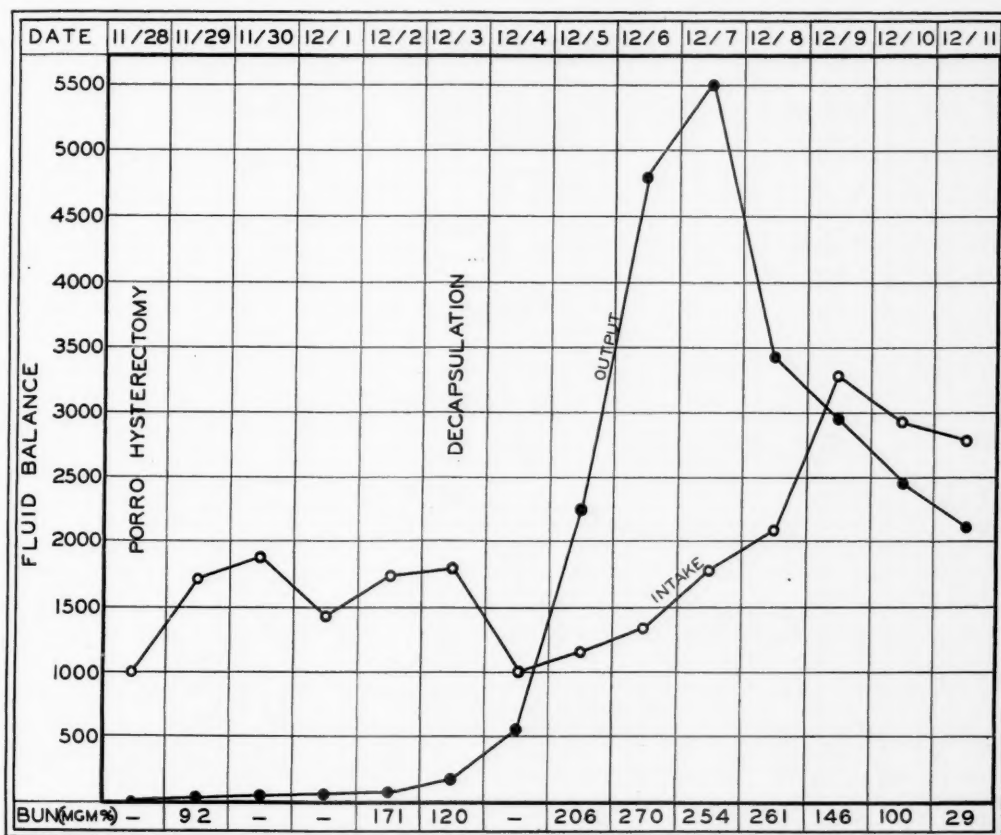


Fig. 3.—Case 2.

Because of the long closed cervix and the persistence of vaginal bleeding, it was thought best to deliver this patient abdominally; and a Porro cesarean section was done. (A typical picture of uterine apoplexy was found at the time of operation.) During the first twenty-four hours after operation, the patient excreted no urine. During the following four days, the urinary output varied between 65 and 90 c.c. daily. The urine specimen

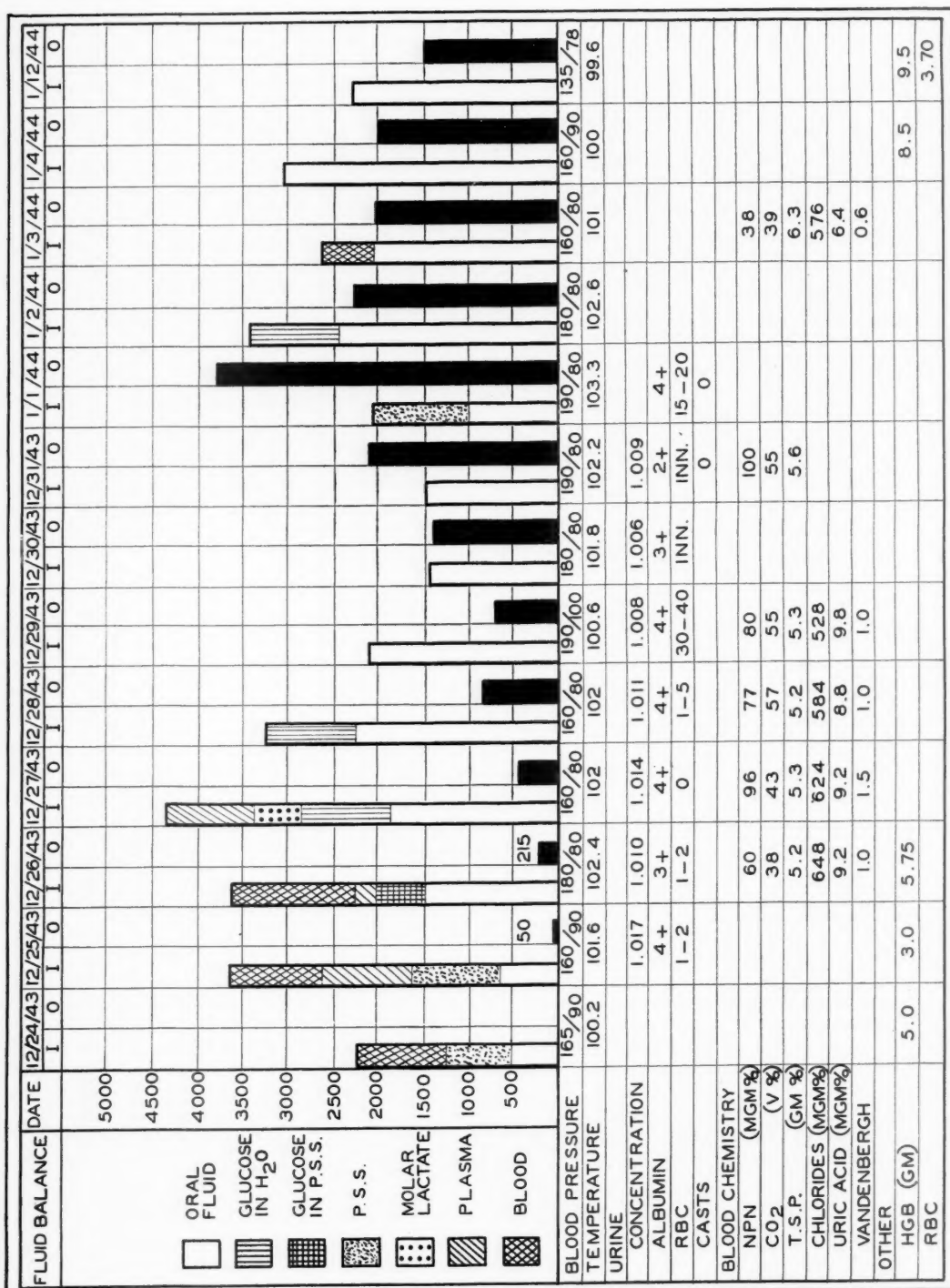


Fig. 4.—Case 3.

on the day following the operation showed a one plus albuminuria and numerous fragmented red blood cells. Because of the oliguria and mounting blood urea nitrogen, a bilateral renal decapsulation was done on the fifth postoperative day. Following this procedure, the patient began to excrete urine; and on the first postoperative day, she passed a total of 635 c.c. On the second day, a total of 2,250 c.c. was voided. She subsequently went on to recovery. Fig. 3 shows the intake and output as well as the blood urea levels.

*Biopsy Report.*—The outstanding finding in this case is the presence of hemoglobin casts within the lower portions of the nephron. In these areas there is atrophy of the tubules of varying degrees. The interstitial tissue in the immediate vicinity is edematous and is infiltrated with mononuclear cells. The upper portions of the nephrons are dilated, and in some instances show minimal atrophy. Focal areas of scarring and capsular thickening are noted. The findings in this material are compatible with a lower nephron nephrosis and are of the type that has been described in "transfusion kidneys."

This patient showed a remarkable recovery following renal decapsulation. Whether her renal lesion was due to the transfusion reaction or premature separation is open to debate. The shock, premature separation, and transfusion reaction provide an excellent background for lower nephron nephrosis. The removal of the uterus should have been followed by some improvement since the source of the chemical toxins was removed. In all probability, however, the process was sufficiently advanced that hysterectomy offered little benefit to the patient. It is also of interest to note that her fluids were restricted.

CASE 3.—Mrs. B. A. C., NCBH No. 24129. The patient was a 25-year-old, white, gravida iv, para i, admitted to the North Carolina Baptist Hospital on Dec. 24, 1943. The calculated date of confinement was Feb. 20, 1944. The patient had made two visits to our prenatal clinic. She had gained 24 pounds in weight, blood pressure 142/80, occasional severe headaches. A salt-free diet and magnesium sulfate by mouth were prescribed, and she was sent home. At 8 A.M. on the day of admission, she began having labor pains and soon began to bleed profusely. She was admitted to the hospital at 4 P.M. with only slight external bleeding.

Examination at this time revealed an acutely ill, pale, quiet woman. The uterus was quite firm and tender. No fetal heartbeat was present. No vaginal examination was made at this time, but a rectal examination revealed the presenting part to be high, and the cervix to be soft and 2 cm. dilated. At the time of admission, the patient's temperature was 100.2° F., pulse 140, respiration 32, blood pressure 165/80, and hemoglobin 4 Gm.

The diagnosis of premature separation of the placenta was made. The patient received 1,000 c.c. of whole blood. Because of multiparity with a favorable cervix and the fact that the patient tolerated the blood loss well, conservative measures consisting of constant observation and Pituitrin stimulation with two minims every 30 minutes for four doses were decided upon in anticipation of a vaginal delivery. The patient had no labor pains following this but continued to have some slight vaginal bleeding. The following morning, the hemoglobin was 3 Gm. Therefore, delivery was effected by cesarean section eighteen hours after admission. A stillborn male infant was delivered. A huge blood clot was found behind the placenta. Blood had infiltrated the uterine wall and broad ligaments, but the uterus contracted following the delivery of the fetus and placenta and was closed in the usual manner.

The patient received 500 c.c. of blood prior to operation and 500 c.c. of plasma during the operative procedure. She was catheterized at 9 P.M. on the 25th, 29 hours after admission, and only 50 c.c. of urine was obtained. The patient had received a total of 5,800 c.c. of fluids since admission. This urine specimen showed a four plus albumin and only an occasional red blood cell. In the next nine hours, only 40 c.c. of urine was obtained and fifteen hours later, 175 c.c. The amount of fluids and the quantity with the output may be seen in Fig. 4.

The patient received large amounts of fluids daily, although she was described as being quite edematous on her first postoperative day. Definite signs of pulmonary edema were observed on the twenty-seventh and the patient was digitalized on the twenty-eighth. The patient was desperately ill on the thirtieth and thirty-first of December; and on January 1, 700

c.c. of serosanguineous fluids were removed from the right chest. The following day another 650 c.c. were removed; and four days later 200 c.c. were removed. The patient had quite a stormy convalescence with a markedly febrile course and received sulfadiazine until the twelfth postoperative day. Numerous transfusions, plasma, and a diet high in proteins and vitamins were also utilized. Blood chemistry gradually returned to normal, and she was discharged on the thirty-second postoperative day with a hemoglobin of 11 Gm. and a trace of albuminuria.

Two things interest us in this case: (1) recovery when the Couvelaire uterus was not removed, and (2) indiscriminate use of intravenous fluids with recovery from oliguria but subsequent cardiac failure and hydrothorax.

We are indebted to Dr. T. D. Tyson, Jr., for permission to use one of his private cases in the following discussion.

CASE 4.—Mrs. Z. W. HP47125. The patient was a 29-year-old primipara with an expected date of confinement March 14, 1947. She was admitted to the High Point Memorial Hospital Jan. 23, 1947, because of hypertension, albuminuria, and excess weight gain. The essential laboratory data are included in Table IV. She went into labor spontaneously on Jan. 29, 1947, delivering a premature stillborn infant at 10:30 P.M. Premature separation of the placenta had been suspected even in the absence of vaginal bleeding and the renal suppression was detected at delivery when only an ounce of urine was obtained, on catheterization (the only output that day).

TABLE IV

DATE	INTAKE C.C.	OUTPUT	SP. GR.	ALBU-MIN	R.B.C.	W.B.C.	CASTS
1/23/47	2,500 oral	1,500 c.c.	1.005	3+	1-2	80-100	0
1/29/47	3,000 plasma 1,000 blood	30 c.c.	1.008	4+	40-60	5-8	5-6
1/30/47	2,000 blood 1,000 5% in H <sub>2</sub> O	490 c.c.	1.008	2+	70-80	50-60	1-2
2/10/47	2,500 oral	1,500 c.c.	1.008	0	1-2	0	0

Postpartum hemorrhage followed and persisted in spite of oxytocics, uterine packing, and adequate replacement of blood. It was necessary to do a hysterectomy to control the bleeding. Shock was mild. From 10:30 P.M., January 29, to 7:30 P.M. the following day, only 120 c.c. of urine were excreted in spite of an intake of 7,000 c.c. during this period.

The microscopic findings in the urine definitely indicated renal pathology of a nature not seen in uncomplicated dehydration. There is, of course, the possibility that in this case, the renal shutdown was secondary to a transfusion reaction. There was no indication of any systemic reaction, no hematin crystals in the urine, and the recovery was most rapid for such an accident. The blood, on rechecking, was found to be compatible. We, therefore, feel that this patient had premature separation of the placenta with extravasation of the blood into the myometrium leading eventually, with the shock, to renal suppression. The subsequent hysterectomy may have removed the source of the chemical toxins, thus assisting in the recovery of the patient.

CASE 5.—Mrs. M. S. H., NCBH No. 50536. This patient was a 30-year-old primipara referred to the North Carolina Baptist Hospital on April 7, 1946, with the chief complaint of edema, albuminuria, and high blood pressure. Her expected date of confinement was June 5, 1946. In January, 1946, she was seen by her family physician because of swelling of the legs. The edema became worse in February. She was referred to a local hospital. At that time, she had edema of the entire body with a one plus albuminuria. The blood pressure varied between 160/100 to 180/120. She was placed on a salt-free diet, bed rest, Nembutal sedation, intravenous and oral fluids to 2,500 c.c. daily. She failed to respond to this therapy and was sent to the North Carolina Baptist Hospital for further treatment.



On admission, her temperature was 100.8° F., pulse 100, respirations 20, blood pressure 180/110. There was a three plus albuminuria. The patient was well developed, with generalized edema. The heart and lungs were normal. Ophthalmoscopic examination revealed some blurring of the right disc, and vasospasm of the retinal vessels. The abdomen was gravid with a one plus edema of the abdominal wall. The uterus was enlarged to the level of the umbilicus and a fetal heartbeat was present in the right lower quadrant. Rectal examination revealed marked edema of the labia, vertex presentation, station plus two with the cervix not effaced or dilated. The essential laboratory and clinical data are recorded in Fig. 5.

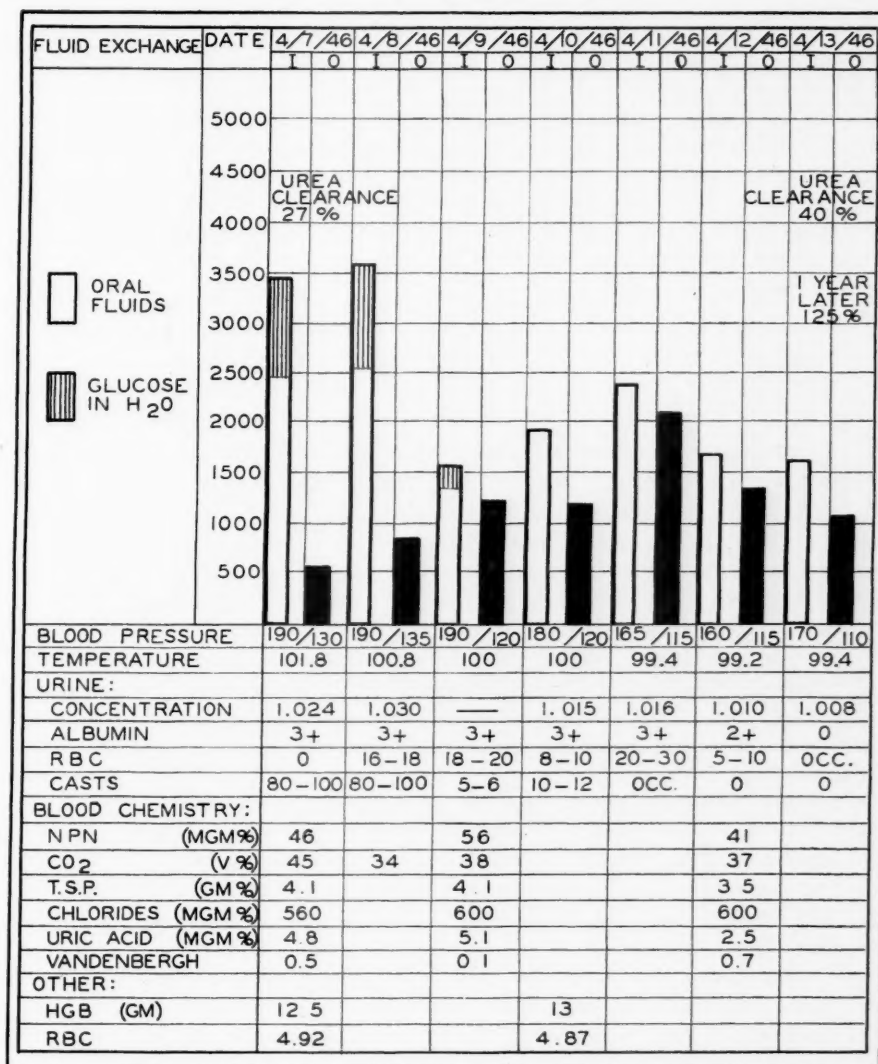


Fig. 5.—Case 5.

The patient was placed on sedation and a high-protein, low-salt diet. In addition, 1,000 c.c. of 20 per cent glucose in water were administered slowly by the vein. The patient developed more edema, became comatose, and distended. The blood pressure ranged from 180 to 190 over 120 to 130. On the second hospital day, the fetal heart sounds disappeared and the urine became grossly bloody. A rectal examination revealed the cervix to be completely effaced, dilated 1.5 cm., and with the head at a station minus one. At 10:30 P.M., the patient

began to put out clear urine in rather large amounts (a total of 200 c.c. accumulating in one hour). The total output up to this point had been only 400 c.c. On her third day, the blood pressure was noted to be dropping, her treatment with sedation and hypertonic glucose solution was continued. There were râles at the bases of both lungs, and the patient began to complain of severe epigastric pain. The situation was complicated by marked abdominal distention. On her fourth day, she began to complain of pains in the lower part of her back, and was considered to be in labor. The labor progressed rapidly, lasting a total of four hours, terminating in delivery of a 3 pound, stillborn female infant. The third stage was uncomplicated.

Following delivery, the patient's blood pressure ranged from 155/100 to 150/90. She felt better and appeared to be improved. Her urinary output rapidly rose, and her blood pressure fell to normal.

Although no accurate record of this patient's intake and output is available prior to her admission to the North Carolina Baptist Hospital, we are certain that her intake was sufficient to produce an adequate output. We feel, therefore, that the low renal output for the first forty-eight hours, the laboratory findings, and the increasing edema indicated renal suppression. Following fetal death, immediate recovery ensued, clearly indicating that the renal damage was of the reversible type. Complete recovery was proved by repeated urea clearance studies over a period of one year:

April 8, 1946	27 per cent average normal function
April 15, 1946	40 per cent average normal function
Dec. 2, 1946	83 per cent average normal function
April 2, 1947	125 per cent average normal function

CASE 6.—Mrs. L. S. M., NCBH No. 47579. A 39-year-old gravida ii, para i, was admitted to the North Carolina Baptist Hospital Jan. 7, 1946, with an expected date of confinement April 23, 1946. Since the onset of her pregnancy, she had been seen regularly by her local physician who stated that she had a normal blood pressure and negative urine specimens. She was picked up in the hospital corridor, after having fainted. She gave a history of severe headaches, dizzy spells, and spots before the eyes for seven days before admission.

On admission, her temperature was 98.6° F., pulse 92, respiration 20, and blood pressure 170/90. She was a well-developed and nourished woman who showed a slight amount of generalized edema. The heart and lungs were negative. The abdomen was gravid with the fundus measuring 18 cm. She was placed on bed rest, salt-free, high-protein diet and phenobarbital sedation. Her blood pressure fell to 130/80 and remained there. She was discharged after eleven days.

She was readmitted on Feb. 7, 1946, because of a blood pressure that was 190/110 and a two plus albuminuria. Examination, with the exception of the blood pressure, was essentially unchanged. She was placed on the routine pre-eclamptic regime. On Feb. 10, she complained of blindness, nausea and vomiting, and examination revealed her blood pressure to be 210/115. There was marked spasm of the retinal vessels and some blurring of both discs. Sodium Amytal was given as a sedative, and a retention catheter was inserted into the bladder. Throughout the day, there was only a scanty reddish-brown output of urine.

On February 11, her blood pressure came down to 150/100. During a twelve-hour period on the eleventh, the patient excreted only 60 c.c. of urine. Intake, output, blood chemistry, urine, etc., may be observed in Fig. 6. On the following day, there was a definite increase in the urinary output. Hypertonic glucose solutions and sedation were continued.

On the afternoon of February 12, a Braxton Hicks version was carried out, and two hours later the patient was delivered of a 2 pound, 3 ounce stillborn male infant. The third stage was uneventful. Her intake on that day was 180 c.c. of 50 per cent glucose, due largely to the fact that no plan of therapy had been devised, and her intake was almost completely overlooked. Following delivery, her blood pressure ranged between 130 and 140 over 98 and 102. On February 13, she was given hypertonic glucose, both 50 and 20 per cent, and she began to pass large amounts of urine, 800 c.c. in one two-hour period (Fig. 6).

She returned on April 10 for a follow-up examination. Her blood pressure was 180/100. A tubal ligation was carried out on June 17, at which time she still exhibited a mild hypertension.

This patient appears to represent a case of essential hypertension. While under medical treatment, the urine became scanty and reddish-brown in color, and a radical termination of the delivery was selected. The outcome would seem to support the decision.

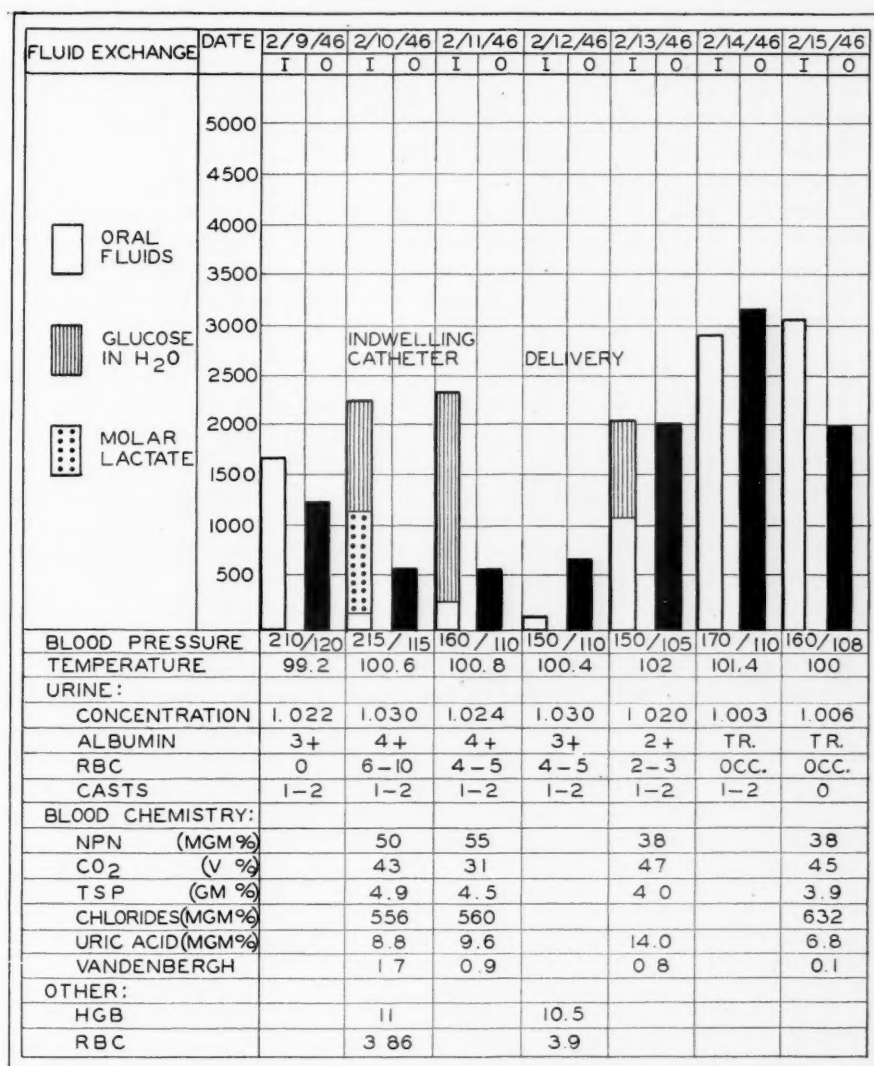


Fig. 6.—Case 6.

**CASE 7.**—Mrs. C. L. S., NCBH No. 49439. This patient was a 35-year-old primigravida admitted on Oct. 15, 1946, with an expected date of confinement on Nov. 27, 1946. Twin pregnancy was diagnosed Aug. 9, 1946. She was referred to this hospital for further prenatal care and delivery. On October 15, her blood pressure was found to be 150/90, and there was a heavy trace of albumin in the urine.

She was admitted to the hospital the following day. Her blood pressure remained around 120/90 with occasional readings going as high as 150/100. She had a persistent

albuminuria ranging from one to two plus. Her intake and output remained normal. Blood chemistries on October 24 were normal with the exception of the uric acid which was 19.2 mg. per cent.

On November 5, she developed a three plus albuminuria with no change in her blood pressure. On the morning of November 8, a urine specimen revealed a specific gravity of 1.010, three plus albuminuria, many finely granular casts. In the afternoon, another specimen revealed a specific gravity of 1.009 with a three plus albuminuria and 20 to 30 red cells with many casts. A cesarean section was decided upon since the cervix was unfavorable for a vaginal delivery. A grossly bloody urine specimen of 10 c.c. was secured just prior to operation. This was loaded with red cells and contained many casts. The delivery was uneventful. Two viable fetuses were delivered and a third macerated stillborn fetus was found. There was at no time any suppression of the urinary output. The red cells, casts, and albuminuria gradually disappeared. With the exception of her uric acid, the blood chemical studies have all been within normal limits.

This patient is of interest because she rapidly developed evidence of severe renal injury. As soon as it became evident that the lesion was progressing, the pregnancy was terminated by operative delivery and prompt recovery occurred. The delivery, like the fetal death in Case 5, probably eliminated the source of the nephro-toxin. In this case, the renal lesion was detected at the first sign of progression.

CASE 8.—Mrs. C. H. W., NCBH No. 49887. The patient was a 20-year-old, white primipara admitted on March 19, 1946, having had three convulsions prior to admission. Her expected date of confinement was March 22, 1946. This patient had received no prenatal care.

Her blood pressure on admission was 170/120 and the urine contained a four plus albumin, hyaline casts, 6 to 8 red blood cells, and 26 to 28 white blood cells. The uterus was gravid and appeared to be at term with a vertex presentation. The fetal heartbeat was heard in the right lower quadrant. The patient was quite irrational and disoriented, and was treated conservatively with intravenous fluids, sedation, and rest.

On the day of admission, her intake was 980 c.c. and her output 270 c.c. On the second day, her intake was 3,230 c.c. and output 1,410 c.c. On the third day, the patient began to show definite signs of oliguria and in a period of eight hours, passed only 50 c.c. of dark bloody urine after having received approximately 1,500 c.c. of 10 per cent glucose in water several hours prior to this. Her blood pressure continued to rise in spite of conservative treatment and because of this, plus the urinary findings, a low corporeal cesarean section was performed and a 6 pound, 13 ounce living male infant was delivered. Four hours after delivery, the output of urine became adequate and remained good. The patient was discharged on April 10, her twenty-third hospital day.

This patient was a severe eclamptic and did not improve under conservative treatment. She was delivered by cesarean section because of rising blood pressure and oliguria with immediate recovery from oliguria after the delivery. Had the delivery been delayed, the kidney lesion might have become irreversible.

CASE 9.—Mrs. D. F. F., NCBH No. 60208. This patient was a 24-year-old primipara who was admitted to the North Carolina Baptist Hospital on Dec. 16, 1946, because of severe hypertension. Her calculated date of confinement was Jan. 1, 1947. She had developed generalized edema and marked weight gain during the past three weeks.

Examination on admission revealed a blood pressure of 170/100 and a three plus pitting edema of the extremities. The abdomen was gravid near term, presentation vertex. The urine contained a two plus albumin and occasional granular cast. Her blood chemistry showed a uric acid of 5.8 mg. per cent, carbon dioxide combining power 43 volumes per cent, non-protein nitrogen 33 mg. per cent. Her weight was 238 pounds.

The patient was placed on conservative treatment consisting of sedation and salt free diet. During the first week with this conservative treatment, her blood pressure became fairly well established at 140/100 and the albuminuria decreased. The intake and output during



this time was adequate. On December 24, eight days after admission, her blood pressure was 150/110, and her output was only 250 c.c., in spite of an intake of 2,450 c.c. The following day, her blood pressure was 170/120, urinary output 100 c.c. with an intake of 1,950 c.c. At this time, no fetal heartbeat could be heard. On December 26, labor was induced by artificial rupture of the membranes, and the patient was delivered nine hours later of a 9 pound still-born child under pudendal block by means of low forceps.

Two hours after delivery, the patient developed severe pulmonary edema, and her blood pressure dropped to 120/60. She was treated with phlebotomy, 1,000 c.c. of blood being withdrawn, oxygen, aminophyllin, and digitalis.

On the day of delivery, she had an output of 500 c.c. with an intake of 550 c.c., consisting mainly of hypertonic glucose. The day following delivery, her intake was 4,095 c.c. and output was 1,200 c.c. The latter remained adequate until the time of discharge on January 10. Blood pressure on discharge was 120/70. The only abnormal blood chemistry finding was a uric acid of 11.5 mg. per cent.

This case would seem to demonstrate how easily oliguria might arise even with the patient under observation and apparently showing improvement in her toxemia. The drop in blood pressure following delivery may have been due to release of the vasoconstrictor forces. As a consequence, the increased renal blood flow would tend to promote increased renal secretion.

### Treatment

It is of prime importance in treating toxemia of pregnancy to watch the intake and output of fluids and maintain a suitable chemical and fluid balance. Should the output of urine, in spite of an adequate intake, descend to oliguric or anuric levels, the uterus should be emptied immediately. Fortunately, in the majority of cases, provided that secondary factors such as hemorrhage, liver damage, trauma from difficult delivery, or sudden fall in blood pressure are absent, the normal physiologic processes will maintain an adequate urinary output.

However, oliguria or anuria persisting after delivery or associated with one or more of the previously mentioned secondary factors is a most serious complication. One is now dealing with a kidney lesion which may be severe or may, if further insulted by too heroic measures, prove irreversible. However, the kidney, like other organs, if given time and proper treatment, may repair the damage and its function be restored to normal.

Treatment must be directed so that the tubular cells have an opportunity to regenerate while maintaining the blood electrolyte balance. Treatment is always controversial when the disease process is not completely understood. We recognize that differences of opinion exist.

Fluids should be restricted to 1,500 c.c. in any twenty-four hour period (including blood, intravenous fluids, and those taken by mouth) unless there are indications for greater amounts, such as blood loss. A kidney that is already swollen and edematous will only become more waterlogged when an attempt is made to break the so-called blockage by forcing fluids. It should be remembered that the mechanism of suppression is not faulty glomerular excretion but rather almost total resorption of fluids from the diseased distal convoluted tubules. Therefore, excessive fluids will be retained until tubular function recovers. Excessive fluids alone are probably the most frequent cause of death in lower nephron nephrosis. Lattimer<sup>6</sup> had seven cases of anuria which recovered when fluids were restricted to 1,000 to 1,300 c.c. When fluids were forced to 3,500 to 6,000 c.c., 75 per cent of the patients died with frank edema and cardiac failure. Kugel<sup>7</sup> reports two cases with severe oliguria (carbon tetrachloride poisoning and transfusion reaction) which recovered under a regime that consisted mainly of limiting fluids.

Hypertonic glucose may be of value prior to the onset of oliguria but fails once real anuria has set in. If given before tubular failure, hypertonic solution may result in increased blood volume and increased renal blood flow. After this point, it is of no benefit in the production of increased renal blood flow. However, carbohydrates protect liver function and should be continued in restricted amounts regardless of the renal output.

Ureteral irrigation has been advocated in the past, but this practice is of questionable value. However, it is essential to make a thorough study of the lower urinary tract in order to exclude an obstruction as cause of anuria.

Renal decapsulation has many enthusiastic supporters. Peters<sup>8</sup> lays great stress on increased intrarenal pressure with reduced renal blood flow as a cause of anuria and states that this is relieved by freeing the kidney capsule. Perhaps it is not only the release of pressure but also an interruption of the vasoconstrictive action, due to the removal of sympathetic nerves between the capsule and cortex, that increases renal blood flow. Fisher<sup>9</sup> states that the capsule is a reflex regulating apparatus for blood flow through the kidney and that decapsulation produces a renal sympathectomy. To be of value the procedure should be done early, before the process becomes irreversible.

Peritoneal irrigation was unknown to us at the time of our patient's death but has been used recently in our hospital with dramatic results following a severe blood transfusion reaction. Grossman, Ory, and Willoughby<sup>10</sup> report the recovery of a postpartum woman with anuria and azotemia of eight days' duration by this means. Streat, Korenberg, and Portnuff<sup>11</sup> had a similar experience with a postpartum patient who developed a transfusion reaction, and severe anuria. The use of the peritoneal cavity as a substitute for the kidney in the removal of metabolic products offers a new concept in the treatment of anuria and may prove lifesaving to many patients who would previously have succumbed.

Repeated blood chemistry studies must be made on all anuric patients and attempt made to control the blood chemical balance. This is particularly important in those patients who are having peritoneal irrigation.

Routine digitalization of these patients may prevent pulmonary edema and congestive heart failure which is the immediate cause of death in most cases. One must also remember that, even if fluids are restricted, occult accumulation of fluid may occur due to marked tissue destruction and give rise to congestive failure. Other supportive measures such as oxygen are always of value.

Our procedure of treatment on anuria may be summarized as follows: (1) limitation of fluids, (2) maintenance of normal blood chemistry, (3) ureteral irrigation, (4) renal decapsulation, (5) peritoneal irrigation, and (6) supportive measures.

### Conclusions

1. Oliguria and anuria present a most serious complication in toxemia of pregnancy. Recent obstetric literature has failed to give this clinical picture its proper recognition.

2. The incidence in our series of toxemia over a five-year period was 5 per cent, with one death.

3. The etiology is still unknown but recent experiences with crush syndrome, transfusion reaction, etc., have yielded much information.

4. Pathology is limited mainly to the lower nephrons although other kidney lesions may be present as the disease progresses. The tubular cells have the power to regenerate after injury.

5. The pathogenesis involves many factors, none of which acting alone seem to be responsible but acting together render the tubular cells susceptible to injury by certain chemical substances.

6. Nine case histories are presented and discussed.

7. It is our opinion that once oliguria or anuria develops the interruption of pregnancy is mandatory.

8. In view of the tubular damage with leakage of the glomerular filtrate into the blood stream, excessive fluids will lead to cardiac decompensation and pulmonary edema with death; therefore, they must be restricted.

9. Renal decapsulation, in our experience, is of questionable value but is a lifesaving procedure in some cases.

10. Peritoneal irrigation is a valuable procedure; serving as an artificial kidney, it removes the waste products during the period of tubular regeneration.

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## AN EVALUATION OF 354 CONSECUTIVE HYSTERECTOMIES PERFORMED AT THE ORANGE MEMORIAL HOSPITAL\*

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CONSIDERABLE publicity has been given recently to the topic of unnecessary operations. At least two lay publications have sponsored articles quoting prominent surgical authorities and presenting scathing indictments against surgeons in general for their promiscuity in the removal of normal organs. That these charges are true, in isolated instances, no one will deny, but the implication that this deplorable situation is generally prevalent has harmful and dangerous potentialities. Public resentment can conceivably be aroused to the degree that necessary, or even lifesaving, operations may be regarded with an attitude of skepticism, causing undue delay or rejection on the part of the patient. Surgeons have been placed on the defensive by these charges, and we, as gynecologists, must accept our share of the responsibility. Hysterectomy appears to be the operation, in the gynecological field, bearing the brunt of the accusations.

Miller,<sup>1</sup> by questionnaire, has reviewed 246 hysterectomies performed during the first four months of 1945 in ten different hospitals, large and small, in three midwestern states, with a correlation of the symptoms, pelvic findings, and histopathology. His study revealed the startling findings that 30.8 per cent of the organs removed in the series presented no evidence of disease and that in 32.8 per cent the operation was either not indicated or contraindicated. He reaches no definite conclusion in his report, but the inescapable one must be drawn that if his findings represent a cross section of the country as a whole, hysterectomy has attained an unenviable place at the top of the list of unnecessary operations. This offers a challenge to hospital staffs to "look behind the curtain" as Miller suggests, turning on the cold light of scrutiny and taking remedial measures as indicated. This is necessary if we are to retain public confidence and respect.

The present study was undertaken for the purpose of determining the hysterectomy situation at the Orange Memorial Hospital. This hospital is a fully approved 250 bed institution with a well-organized staff and a full-time certified pathologist. It is impossible to make any comparison between this staff and those of the ten hospitals reviewed by Miller, but the fact that all organs removed in those hospitals received a pathologic examination would indicate that they meet at least minimum, or better, requirements. It was hoped that some conclusions could be reached as to whether hysterectomy is an abused operation in the Orange Memorial Hospital, or whether the errors in diagnosis and indications for operations approach that irreducible minimum

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which can be attributed to honest, human mistakes in diagnostic skill and surgical judgment. This latter figure is difficult to compute and will vary with individual interpretation.

### Material

A personal analysis was made of the hospital case records of 354 consecutive hysterectomized patients between April 5, 1946, and Dec. 17, 1947. The date for the beginning of the study was chosen because it coincided with the return of the pathologist to the hospital after a leave of absence. The hysterectomies were performed by 21 different operators, seven belonging to the gynecologic, and fourteen to the general surgical staff of the hospital. The largest number of operations done by one staff member was 113 and the least one. Fourteen members were responsible for less than ten hysterectomies each. Permission was obtained from all the members concerned in the study for a review of their charts with the knowledge that the findings would be reported.

TABLE I. TYPE AND NUMBER OF HYSTERECTOMIES ACCORDING TO AGE GROUPS

TYPE	UNDER 20	20-29	30-39	40-49	50-59	60-69	70-79	NUMBER
Total		12	44	53	11			120
Subtotal	1	19	70	60	12	1		163
Vaginal		3	18	27	14	6	3	71
Total number	1	34	132	140	37	7	3	354

Table I indicates the number and types of hysterectomies according to age groups. The largest number, 140, (40 per cent) was performed, as might be expected, in the group 40 to 49 years of age. This group also contains the greatest number of the total type, 53, or 44 per cent. Thirty-five hysterectomies, or 10 per cent, in patients under 30 years of age appear high, and deserve the closest scrutiny in the final analysis. Nine of the ten cases in the group 60 to 79 years old are of the vaginal type. This is in accord with the accepted trend of the use of the vaginal route in elderly patients.

TABLE II. TYPE AND NUMBER OF HYSTERECTOMIES ACCORDING TO HOSPITAL SERVICE

TYPE	GYNECOLOGIC SERVICE	PER CENT OF 232	SURGICAL SERVICE	PER CENT OF 122
Total	88	38	32	26
Subtotal	81	35	82	67
Vaginal	63	27	8	7
Total number	232	100	122	100
Per cent of 354	65.5		34.5	

The number and types of hysterectomies according to service in the hospital are listed in Table II. The gynecological service showed a preference for the total operations over the surgical group, 38 per cent to 26 per cent. However, when this was broken down, it was discovered that two gynecologists performed 84 of the 88 total type, and three general surgeons 25 of the 32 totals in that service, or that five operators of the 21 did 90 per cent of the total operations. It is evident that both groups as a whole have not accepted the generally asserted advantage of the complete over the incomplete operation, or else have properly recognized their limitations. I am in complete agreement with Miller that the only advantage of the total over the sub-

total operation is in the removal of the diseased cervix. However, since I have personally treated five carcinomas of the cervical stump within the last year, the advantage to me is genuine, and there seems little justification for the experienced operator not to employ the total operation except in difficult cases such as extensive pelvic endometriosis or inflammatory disease, where the safety of the patient might be endangered by the removal of the cervix. I am also sure that the total operation is technically more difficult, and the occasional operator had best confine his hysterectomies to the subtotal type.

The gynecologic staff showed a decided preference over the surgical for the vaginal type, 27 per cent to 7 per cent. However, here again it was found that two of the seven gynecologists did 58 of the 63 vaginal hysterectomies.

There were two deaths in the 354 cases, a mortality rate of 0.7 per cent in the abdominal hysterectomies, or 0.56 per cent in the whole series. Both of these deaths were due to pulmonary emboli, one on the second postoperative day (autopsied), and the other on the eighth day while the patient was in the chair. Both also occurred in the subtotal operations, done by the surgical service. These facts are not considered significant as both deaths were apparently unpreventable.

TABLE III. SYMPTOMS OF PATIENTS

COMPLAINT	NUMBER	PER CENT
Bleeding	148	41.8
Pain, lower abdomen	111	31.3
Dysmenorrhea	73	20.6
Leucorrhea	54	15.3
Backache	50	14.0
Mass, lower abdomen	49	13.8
Secondary symptoms { headache nervousness fatigue weakness, etc.	46	13.0
Urinary symptoms	33	9.3
Bearing down or heavy feeling in the lower abdomen	32	9.0
Prolapse	24	6.8
No symptoms	10	2.8
Dyspareunia	6	1.7
Pregnancy	6	1.7

Table III shows the complaints of the patients at time of examination. Many had multiple symptoms. One hundred forty-eight patients, or 41.8 per cent, complained of abnormal bleeding. This agrees very closely with the figure of 41.4 per cent in Miller's series. Three hundred eight, or 78 per cent, complained of bleeding and/or pain and a mass in the lower abdomen. There is considerable variance in this series in the number of patients who presented no symptoms, 10, or 2.8 per cent, and 43, or 17.4 per cent, in Miller's. I am unable to explain this discrepancy except on the basis of incomplete histories.

In the 354 pelvic examinations (Table IV) fibroids were discovered 205 times, 57.9 per cent. By comparison, Miller found this diagnosis in 31.7 per cent of the cases in his report. The most significant disclosure is the difference between the normal pelvis, reported in these two studies, 2, or 0.6 per cent, in this, and 46, or 18.6 per cent in Miller's. Again, it is difficult to reconcile the fact that normal pelvic findings in the latter group were 30 times greater than in this series. Pregnancy was discovered eight times, and hysterectomy was

performed for various reasons as shown later. Outside of two of these cases, the two normal pelves, and one case of suspected carcinoma of the cervix, where total hysterectomy was contraindicated, there would appear to be no preoperative diagnosis that did not grossly indicate operation. However, the accuracy of these findings remains to be vouched for.

TABLE IV. PELVIC FINDINGS ON EXAMINATION

FINDING	NUMBER	PER CENT
Fibroids	205	57.9
Cervicitis	106	30.0
Prolapse, uterus	60	17.0
Relaxation, perineum	59	16.7
Cystocele	48	13.8
Salpingitis	32	9.4
Ovarian cysts		
Benign	27	7.6
Malignant	2	.6
Rectocele	23	6.5
Retrodisplacement, uterus	18	5.1
Fibrosis uteri	10	2.8
Pregnancy	8	2.3
Endometriosis	7	1.9
Adenomyosis	6	1.7
Cervical polyps	4	1.1
Abdominal adhesions	* 3	.9
Pyometria	2	.6
Ruptured uteri	2	.6
Carcinoma, corpus	2	.6
Normal pelvis	2	.6
Carcinoma, cervix	1	.3
Postpartum uterus (hemorrhage)	1	.3
Tubal pregnancy	1	.3
Intestinal obstruction	1	.3
Leucoplakia, cervix	1	.3

The pathologic findings are divided between the organs removed by the abdominal and vaginal routes and are catalogued in Table V. Fibroids were found 205 times in both groups (57.9 per cent). Peculiarly, this was the exact figure in the preoperative findings. I must reluctantly disclaim this as evidence of supernatural diagnosis and regard it as a coincidence. Miller's figures show fibroids present in 43.4 per cent. Since all of these fibroids were undoubtedly not of sufficient size to warrant operation, it was interesting to note that 170, or 83 per cent, had symptoms of abnormal bleeding, and/or abdominal pain and palpable abdominal mass, generally acceptable criteria for hysterectomy. Of the other 35, 12 were removed by vaginal hysterectomy for reason of prolapse, and of the remaining 23 only four were asymptomatic. There were four uteri diagnosed as normal, twelve normal with the exception of chronic cervicitis, and six normal with the exception of pregnancy. In the abdominal cases, chronic cervicitis per se was not recognized as an indication for hysterectomy. This gives a total of 22 cases, or 7 per cent, in which operation was not justified for lack of pathology. In the 71 vaginal hysterectomies, all cases showed prolapse and/or sufficient uterine pathology to justify operation except two, as will be shown in the final summation, where it was felt the operation was ill chosen. If these 69 cases are included in the total series, the incidence of insufficient pathology or relaxation for operation is reduced to 6.8 per cent. Miller's group of 246 cases, including 12 vaginal hysterectomies, showed no pathology or relaxation in 76 instances, or 30.8 per cent.

TABLE V. PATHOLOGY OF ORGANS REMOVED

FINDING	ABDOMINAL OPERATION	PER CENT OF 283	VAGINAL OPERATION	PER CENT OF 71
Fibroids	180	63.6	25	35.2
Cervicitis	120	42.0	68	95.8
Salpingitis	64	22.6	1	1.4
Ovarian tumors				
Benign	54	19.0	1	1.4
Malignant	4	1.4		
Hyperplasia endometrium	24	8.4	9	12.7
Uteri				
Normal except cervicitis	12	7.7		
Normal except pregnancy	6			
Normal	4			
Endometrial polyps	21	7.4	5	7.0
Adenomyosis	20	7.0		10.0
Pregnancy or retained products	15	5.3		
Endometriosis	9	3.2		
Fibrosis uteri	9	3.2	3	4.2
Cervical polyps	5	1.8	3	4.2
Carcinoma corpus	3	1.1	1	1.4
Myosarcoma	2	.8		
Tubal pregnancy	1	.4		
Postpartum uteri				
Hemorrhage	1	.4		
Rupture	1	.4		
Pyometria	1	.4		
Bicornate uterus	1	.4		
Uterus didelphys	1	.4		

There were 15 cases of pregnancy or retained secundines discovered on pathologic examination. These were analyzed and the results are listed in Table VI.

TABLE VI. PREGNANCY OR RETAINED PRODUCTS FOUND ON PATHOLOGIC EXAMINATION—  
15 CASES

FINDING		NO. CASES RECOGNIZED	NO. CASES UNRECOGNIZED
Hysterectomy indicated, 9 cases	Sterilization for medical indications with consultation	5	
	Retained secundines with fibroids		3
	Fibroids. 6 months' pregnancy. Hemorrhage. Possible rupture	1	
Hysterectomy not indicated, 6 cases	Normal pregnancy		4
	Pregnancy with fibroids. No consultation	2	
Total number		8	7

### Justification of Hysterectomies on Basis of Pathologic Findings

In 237 of the 283 cases of abdominal hysterectomy (83.7 per cent), the pathologic findings confirmed the clinical diagnoses. Removal of the uterus was considered justifiable in all but two of these cases, 235, or 83.3 per cent. In Miller's report, 122 of the 246 cases (49.6 per cent) were confirmed. All of these were considered justifiable. This appears to be a real basis for comparison between the two series. In order not to pad or distort the results, the vaginal hysterectomies (71) are not included in this statistical study, as the indication for operation in this group was primarily prolapse rather than diseased organs. Of the 46 cases in which the clinical diagnosis was not con-



firmed by the pathologist, the operation was considered justifiable in 16, or 5.7 per cent. Miller's figure in this category is 43 cases (17.4 per cent).

TABLE VII. SUMMARY OF JUSTIFIED AND UNJUSTIFIED HYSTERECTOMIES

	ORANGE MEMORIAL'S SERIES 283 CASES		MILLER'S SERIES 246 CASES	
	NO. CASES	PER CENT	NO. CASES	PER CENT
<i>Hysterectomy Justified</i>				
Clinical diagnosis confirmed by pathologist	235	83.3	122	49.6
Clinical diagnosis not confirmed by pathologist	16	5.7	43	17.4
Total	251	89.0	165	67.0
<i>Hysterectomy Not Justified</i>				
Minimal symptoms and pathology	2	.7		
Clinical diagnosis confirmed by pathologist				
Clinical diagnosis not confirmed by pathologist	8	2.7		
No histopathology (or relaxation)	4	1.4	76	30.8
No histopathology except cervicitis	12	4.2		
Diagnosis contraindication to operation (pregnancy or retained secundines)	6	2.0	5	2.0
Total	32	11.0	81	32.8

### Hysterectomies Not Justifiable

This decision presented no difficulty in the four cases showing no pathology, twelve with no pathology except cervicitis and six where the operation was contraindicated because of the sole finding of pregnancy or retained secundines (Table VII). Obviously this did not tell the whole story, for it seemed improbable that there should not be some cases in the remaining 261, where the hysterectomy was not justified. In order to determine this, these 261 records were critically analyzed to discover if the symptoms and pathology present were of sufficient importance to justify extirpation of the uterus. It was realized that this would not be easy, for the clinical record often does not visualize the picture of the patient as a whole, and other factors, known to the attending physician alone, might influence the decision. It is also difficult in absentia to decide what course one would have followed at the operating table, and so, realizing full well that he was treading upon delicate ground and chagrined to discover that he too was not entirely absolved from criticism, the reviewer based his decision for or against justification for the removal of the uterus on these grounds: (1) age of the patient; (2) minimal symptoms; (3) minimal pathology. On this basis, the following cases were regarded not acceptable for hysterectomy.

#### CLINICAL DIAGNOSIS CONFIRMED BY PATHOLOGIST

CASE 1. Age 29. Leucorrhea. Vaginal hysterectomy, primarily for sterilization. Finding, simple hypertrophy of uterus.

CASE 2. Age 29. Menorrhagia. Total hysterectomy. Finding, hyperplasia of endometrium.

#### CLINICAL DIAGNOSIS NOT CONFIRMED BY PATHOLOGIST

CASE 3. Age 30. Abdominal pain. No bleeding. Total hysterectomy. Finding, myoma 0.5 cm.

CASE 4. Age 50. Menopausal symptoms, no bleeding. Subtotal hysterectomy. Finding, small retention cysts ovaries.

- CASE 5. Age 27. Dysmenorrhea. No bleeding. Total hysterectomy. Finding, hemorrhagic cyst ovary. Chronic cervicitis.
- CASE 6. Age 25. Abdominal pain. No bleeding. Subtotal hysterectomy. Finding, benign endometrial polyp.
- CASE 7. Age 35. Dysmenorrhea. No bleeding. Subtotal hysterectomy. Finding, hyperplasia endometrium. Chronic cervicitis.
- CASE 8. Age 47. Leucorrhea. No bleeding. Subtotal hysterectomy. Finding, benign endometrial polyp.
- CASE 9. Age 24. Menometrorrhagia. Subtotal hysterectomy. Finding, multiple retention cysts ovaries.
- CASE 10. Age 36. Dysmenorrhea. No bleeding. Total hysterectomy. Finding benign endometrial polyp.

TABLE VIII. FINAL SUMMATION OF ORANGE MEMORIAL'S AND MILLER'S SERIES

	ORANGE MEMORIAL'S SERIES 283 CASES		MILLER'S SERIES 246 CASES	
	NO. CASES	PER CENT	NO. CASES	PER CENT
Patients with no symptoms	10	2.8	43	17.4
Patients with normal pelves	2	.6	46	18.6
No pathology (or relaxation)	16	5.6	76	30.8
Clinical diagnosis confirmed by pathologist	237	83.7	122	49.6
Clinical diagnosis not confirmed by pathologist	46	16.3	124	50.4
Hysterectomy justified	251	89.0	165	67.0
Hysterectomy unjustified	32	11.0	81	32.8

For a summary of the comparison between the justified and unjustified 283 abdominal (1 vaginal) hysterectomies in this series, and the 246 (including 12 vaginal) in Miller's, attention is again directed to Table VII. The final summation of the two series can be seen at a glance in Table VIII. The main point of interest is that in Miller's study the clinical diagnoses were not confirmed by the pathologist in approximately three times as many cases as in the Orange Memorial Hospital's and the hysterectomy was judged unjustified in about the same ratio. This should emphasize the role of the pathologist as the final arbiter in the justification for any operation where the removal of organs is involved.

### Misuse of Type of Hysterectomy

In a study of this nature, attention should be directed to the cases where hysterectomy was apparently indicated, but the interest of the patient would have been better served by the use of a different type of hysterectomy than the one employed. Three cases, of the 354 reviewed, were considered to fall within this classification and are briefly evaluated as follows.

- CASE 1. Age 53. Irregular bleeding. Vaginal hysterectomy. Finding, adenocarcinoma of the corpus. A preliminary curettage was indicated, followed by radium, and later, total hysterectomy.
- CASE 2. Age 63. Irregular bleeding. Subtotal hysterectomy. Finding, adenocarcinoma of corpus. The same procedure should have been employed as in Case 1.
- CASE 3. Age 36. Prolapse. Total hysterectomy with no vaginal repair. Patient would have been better served by vaginal hysterectomy and posterior colporrhaphy.

Thus, it will be seen that there was a misuse of the type of hysterectomy in 3 of 354 cases, or 0.80 per cent.

### Discussion

It is evident, in most hospitals today, that the indications for hysterectomy have been considerably broadened in recent years. Indeed, in many good medical centers, this operation has almost replaced irradiation in the treatment of benign bleeding at or near the menopause. The factors responsible for this radical trend are well known and need not be repeated. Perhaps the pendulum has swung too far and may be expected to return to a more middle course. The decision for hysterectomy is a serious one, for it involves not only the removal of an organ, but constitutes a major break in the pituitary-ovarian-uterine relationship with possible endocrine and neuropsychogenic upheavals. It is incumbent upon the gynecologist to weigh the decision carefully, using all diagnostic means at his disposal and exercising his soundest surgical judgment. Even so, as Wharton<sup>2</sup> has aptly stated, "in spite of the exercise of our greatest care, in spite of the performance of all pertinent diagnostic procedures, in spite of the fact that we have sought the advice of our colleagues in arriving at the proper conclusions, in spite of all of this, there is not one who has not made unfortunate mistakes." This is not said in defense of indiscriminate hysterectomy, for the removal of a normal uterus without extenuating adnexal pathology or prolapse is to be condemned today as at any time in our gynecologic evolution.

It would seem that the main criticism in this report should be directed toward the number of uteri removed in the younger group, 10 per cent of the total in women under 30, and 46 per cent below the age of 40. This compares closely with the figures found by Miller of 12 per cent and 44 per cent respectively. There is no doubt that this number is too large, and unquestionably some of these cases could have been treated by a more conservative mode of therapy to the advantage of the patient.

What constitutes abuse is difficult to define. To admit this charge, evidence must be produced that there has been undue laxness in indications for operation, that reasonable diagnostic care has not been practiced, and even a hint that remunerative considerations have transcended surgical necessity. With no precedent except Miller's study (32.8 per cent), it is not simple to evaluate an incidence of 11 per cent unjustified hysterectomies. Admitting that this figure is too high and should be reduced, preoperative pelvic findings of 1.4 per cent, in which operation was not indicated or contraindicated, would not appear to suggest a laxness in indications for operation, and confirmation of the clinical diagnosis by the pathologist in 83.7 per cent of the cases would seem to imply that reasonable diagnostic care had been practiced. Therefore, I am disinclined to designate hysterectomy as an abused operation at the Orange Memorial Hospital until more reports of this type are forthcoming from hospitals with well coordinated staffs. Miller is to be commended for his pioneering in this investigation, and it is to be hoped that his effort will stimulate further comparative studies so that the true status of hysterectomy as an operation of necessity can be established.

### Summary

1. A review of 354 consecutive hysterectomies, performed by seven members of the gynecological, and fourteen of the surgical staff, of the Orange Memorial Hospital, is presented.
2. These 354 hysterectomies consisted of 120 total, 34 per cent, 163 subtotal, 46 per cent, and 71 vaginal types, 35 per cent.
3. The greatest number of cases, 140, or 40 per cent, occurred in the age group 40 to 49 years. There were 167 hysterectomies, 46 per cent, performed in women under 40 years of age.
4. The gynecological service was responsible for 232, 65.5 per cent, of these cases and the surgical service 122, 34.5 per cent.
5. There were two deaths in this series, a mortality incidence of 0.7 per cent in the abdominal hysterectomies and 0.56 per cent in the whole group. Both of these deaths were due to pulmonary emboli in the subtotal operations.
6. Ten patients, 2.8 per cent, had no preoperative symptoms. Abnormal bleeding was the chief complaint of 148 patients, 41.8 per cent, and 308, 87 per cent, complained of bleeding and/or pain and mass in the abdomen.
7. Fibroids were discovered 205 times, 57.9 per cent, in the pelvic examinations prior to operation. Only two cases, 0.6 per cent, were reported as having normal pelves. The preoperative findings appeared grossly to indicate operation in all but five cases, 1.4 per cent.
8. Fibroids were found in 205 of the removed uteri, 57.9 per cent, by the pathologist. The uteri removed abdominally were reported normal (including cervicitis and pregnancy) 22 times, 7.7 per cent. Pregnancy or retained products were reported in 15 cases, 5.3 per cent.
9. Of the fifteen cases showing pregnancy or retained products on pathological examination, eight were recognized preoperatively and seven were unrecognized. Hysterectomy is judged to have been indicated in nine of these patients and not indicated in six.
10. The clinical diagnosis was confirmed by the pathologist in 237 of the 283 abdominal hysterectomies, 83.7 per cent, and not confirmed in 46 cases, 16.3 per cent.
11. In 235 cases confirmed by the pathologist, 83.3 per cent, the hysterectomy is considered justified, and in 16 of the unconfirmed cases, 5.7 per cent.
12. Based on the 283 abdominal hysterectomies, the removal of the uterus is considered justifiable in 251 cases, 89 per cent, and unjustifiable in 32, 11 per cent.
13. In three of the total 354 cases, 0.8 per cent, the type of hysterectomy is judged misused.

### Conclusion

From this study it is felt that hysterectomy has been employed too liberally in the past, in the younger group of patients at the Orange Memorial Hospital, and that the incidence of 11 per cent unjustified operations is too high and



should be reduced, but from the low rate of preoperative pelvic findings, 1.4 per cent, in which the operation was not grossly indicated and from the confirmatory pathologic support of the clinical diagnosis in 83.7 per cent of the cases, the abuse of the hysterectomy operation in this particular hospital is not conceded.

The author wishes to express his thanks to Dr. Norman F. Miller for his endorsement of this review and generous permission to use his figures for a comparative study and to those members of the staff of the Orange Memorial Hospital who, in such a fine spirit of cooperation, gave their consent for a review of the hospital clinical records of their patients.

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1503 KUHLE AVENUE

## INVERSION OF THE VAGINA FOLLOWING HYSTERECTOMY\*

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INVERSION of the vagina following hysterectomy has long been recognized as a particularly difficult condition to cure satisfactorily. It is often accompanied by troublesome complications such as cystocele, cystitis, incontinence, which demand relief. Many procedures have been devised to meet the indications. Most of these have depended upon some method of suspending the vaginal vault to the fascia of the abdominal wall as described by Brady,<sup>1</sup> or plication to the broad ligaments as used by Payne.<sup>2</sup> These, of course, depend also upon vaginal plastics. Brady depends on the tension of the anterior vaginal wall to support the bladder and uses only posterior repair of the vaginal tract. These, no doubt, have a field of usefulness. Some can be advantageously repaired by a vaginal plastic alone after the Manchester plan. There is a small group which requires unusual effort.

The purpose of this communication is to describe a procedure which I have developed and used with satisfaction. As far as I know, this plan as used has not been previously described. I offer this as one addition to the armamentarium available for the treatment of this difficult problem.

On July 22, 1944, I was consulted by a patient who presented a condition which would obviously place a considerable strain on any method of repair used. The patient was 66 years of age, had been married forty-six years, and had four children. A complete hysterectomy had been done at the age of 39, or twenty-seven years before. Her general physical condition was good except for diabetes which was then being controlled by diet. The chief complaint was the protrusion of a mass of considerable size which obviously contained bladder and intestines as well as rectum. The bladder symptoms were troublesome. There was not only bladder frequency but partial incontinence. Although the prolapse had existed over several years, there was no ulceration but the mucous membrane was thick and hypertrophied. There was nothing to show where the cervix had been except a scar or dimple. The perineal supports were practically worthless.

While reviewing available literature, my attention was called to the Berkeley-Bonney<sup>3</sup> modification of the Le Fort operation which seemed to offer advantages over the usual Le Fort, but this or any other method of suture of the vaginal wall would not be expected to give the needed support to cure such a hernia as this. In fact, I did not find that any method which I had used or with which I was familiar gave promise of satisfactory relief. However, this modification of the Le Fort would answer well as a final step after the anterior and posterior vaginal plastic.

\*Read at the Tenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Augusta, Ga., Feb. 12 to 14, 1948.

### Technique

The technique used consisted first of the usual dissection of the anterior vaginal wall and the pubocervical fascia as shown in Fig. 1. The inverted vault is grasped by a tenaculum at the point where the cervix was removed and the structures placed in slight tension. A short transverse incision is made about an inch from this, then by blunt-scissors dissection the vaginal wall is separated from the pubocervical fascia to a point near the meatus. Prolapse, of course, makes the dissection of the anterior vaginal wall particularly easy. The vaginal wall is separated from the pubocervical fascia first by sharp dissection and then by gauze-covered finger the fascia is exposed as far laterally as needed and carried backward to the scar tissue which originally represented the broad ligaments. Sutures are started near the urethra and carried back to the original site of the cervix. The end of this consists of structures remaining from the broad ligaments. When the fascia was dissected far to the sides, the support was surprisingly strong. Altogether, this gave a shelf of very definite strength which not only held the bladder up but contributed to the pelvic support. Mattress stitches are placed over the urethral sphincter and urethra and give support to these structures. The vaginal flaps are not removed but left for suture as a part of the last step in the operation.



Fig. 1.—Dissection of anterior vaginal wall. Separation of pubocervical fascia. Fascia freed from pubic rami and vaginal mucosa.

The posterior structures are dissected in much the same way as the anterior. A tenaculum is placed on either side of the vaginal tract just below the opening of the Bartholin ducts and placed on slight tension. A strip of tissue connecting these points is removed at the mucocutaneous junction with

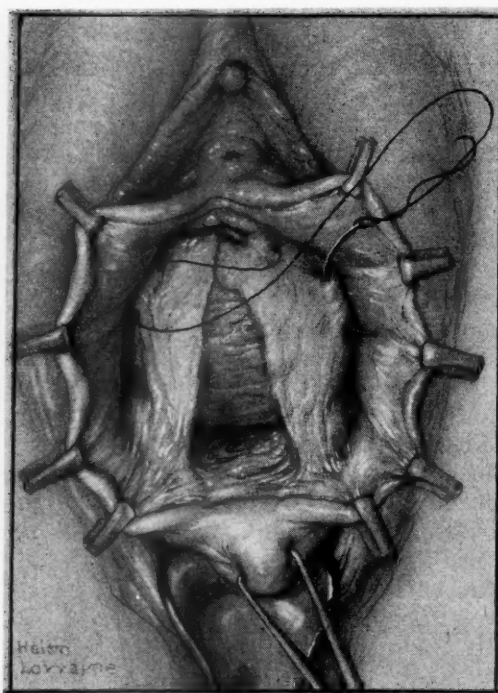


Fig. 2.

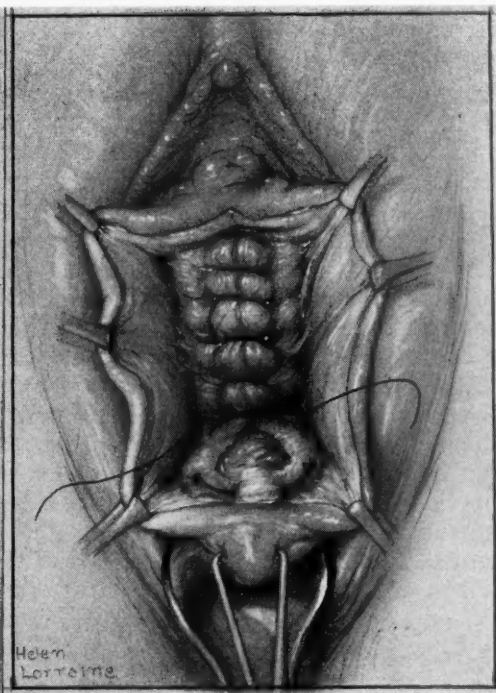


Fig. 3.

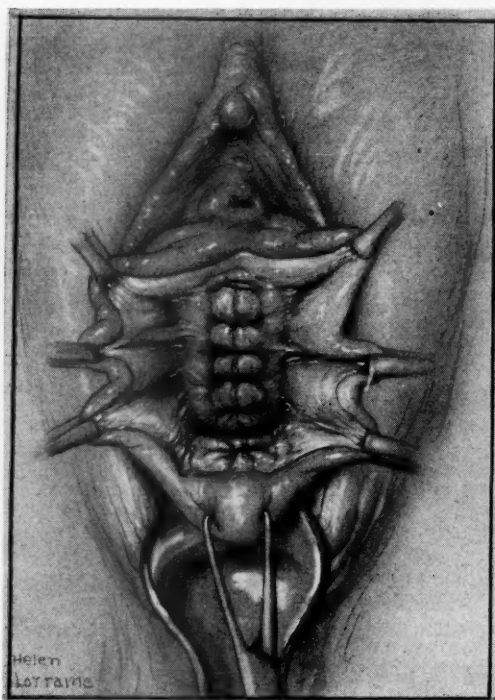


Fig. 4.

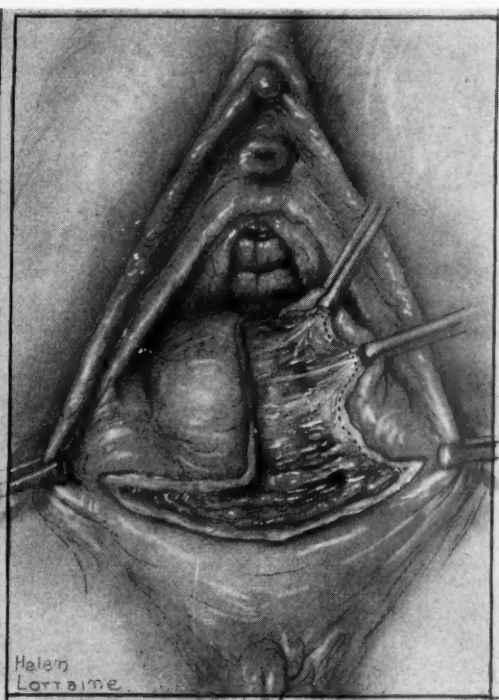


Fig. 5.

Figs. 2, 3, and 4.—Tightening of pubocervical fascia using continuous suture and several mattress sutures for reinforcement.

Fig. 5.—Dissection of posterior vaginal wall. Separation of rectovaginal fascia from vaginal mucosa.



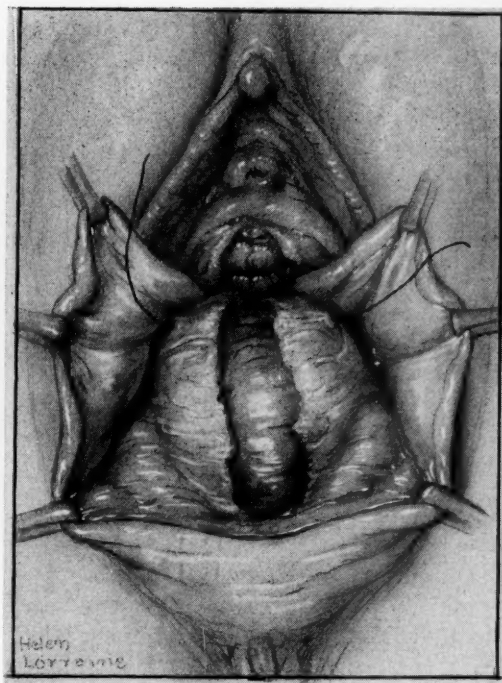


Fig. 6.

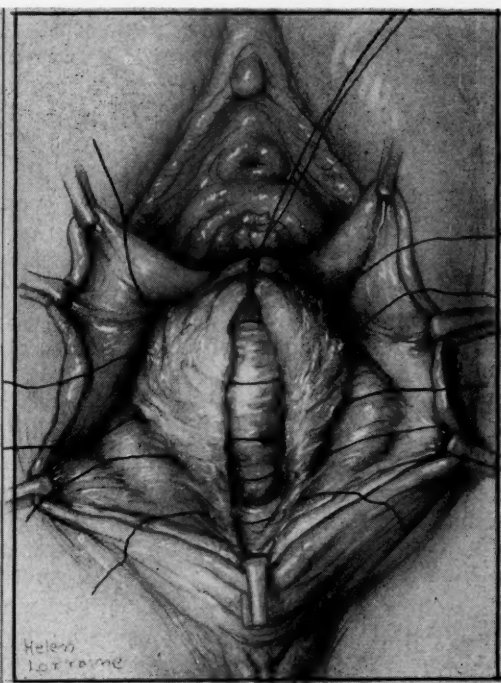


Fig. 7.

Figs. 6 and 7.—Suture of rectovaginal fascia.

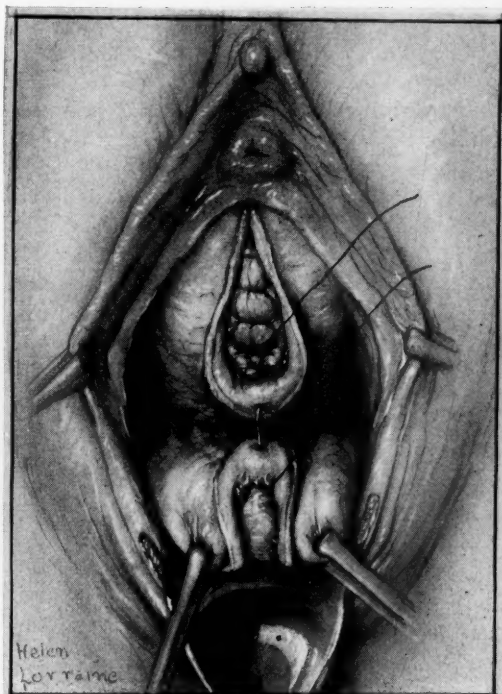


Fig. 8.

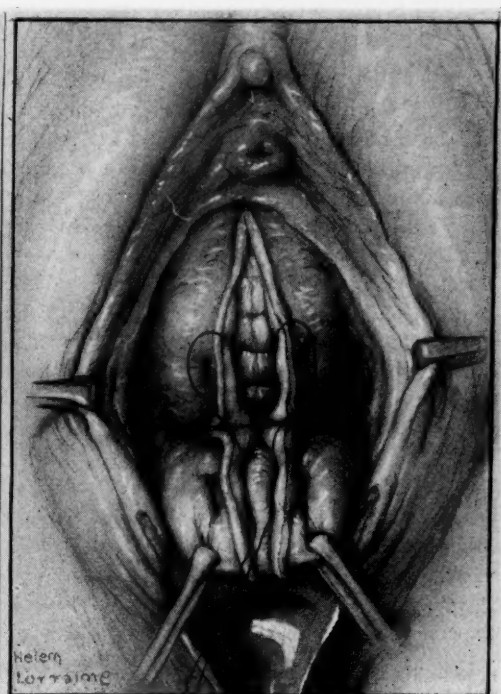


Fig. 9.

Fig. 8.—Initial suture approximating anterior and posterior vaginal walls. No vaginal mucosa is excised.

Fig. 9.—Approximation of incised areas of anterior and posterior vaginal walls by mattress sutures tied inside forming median septum. Each suture carries apex higher.

scissors. The posterior vaginal mucous membrane is separated by scissors dissection to a point about an inch from the tip of the vaginal vault. The vaginal flaps are dissected to the sides first by sharp dissection and then by gauze-covered finger. These are carried to a point where the rectovaginal fascia is clearly seen and felt. At this point the enterocele was encountered and was dissected, tied off, and excised. This, of course, has nothing to do with this particular method except that it was encountered in this case. The rectovaginal structures are closed by interrupted stitches beginning near the anterior end of the dissection. These stitches are carried to the end of the perineum near the rectum as shown in Figs. 6 and 7. The levators are now sutured (Figs. 9 and 11). At this point the Berkeley-Bonney method of closure of the Le Fort is used, as shown in Figs. 8 and 10. All four flaps, two anterior and two posterior, are brought together by a sufficient number of mattress sutures beginning at the top, each one carrying the previous one higher. Then the suture described as the "crown stitch of Emmet" is carried from the left side of the original incision through such structures available including the levators; when this is tied it raises the perineum high (Fig. 12). This is augmented by any stitches which may be necessary. The skin of the perineum is closed by a fine catgut running stitch which is continuous with the final closure of the mucous membrane. At the completion of the operation, the vaginal tract has the appearance of being entirely normal in support except that the tract is a double-barrel affair communicating at the distal end. This has very much the appearance of a double vagina. When seen recently, this patient stated that she has no symptoms of any sort referable to the pelvis. Although nearly 70 years old, she is carrying on the heavy duties of a boardinghouse keeper. In all respects, the results were perfect.

This procedure is also useful for a large, complete prolapse when there has been no hysterectomy but the uterus and cervix are so atrophied as to be of only slight use.

This is illustrated by a patient who was seen first on June 3, 1945. She was 76 years old, had been married fifty years, and had had six full-term pregnancies, youngest child aged 37 years; all deliveries were said to be normal. This patient was short, rather obese, with pendulous abdomen. Her chief complaints were persistent bladder symptoms and protrusion of a mass from the introitus. This mass also was of considerable size and seemed to consist principally of cystocele but when she stood on her feet the whole vaginal tract inverted. The cervix was represented by a little more than a dimple as these structures were severely atrophied. When first seen, the urine contained considerable pus and the history recorded that the bladder symptoms had been most persistent for a long time. Hypertension was moderate, 176/86. This patient is a portrait painter and likes to be on her feet a considerable part of the day. This fact, no doubt, contributed to the cause of the prolapse and also increased the demand for relief. Every manner of support was tried for her but as the levators were worthless, none of them were of any particular value. The operation was done on Oct. 22, 1946. The technique was essentially the same as in the previous case except that there was a small cervix to which the attenuated cardinal ligaments were attached. The cardinal ligaments were brought anterior to this and sutured, which helped the plan considerably. The posterior vaginal structures were dissected as in the previous case. This hernia also was so large that it was not felt that the fascia would be sufficiently strong to hold it alone. So the vaginal flaps were sutured after the Berkeley-Bonney plan. Anesthesia used in this case was Pentothal sodium. We now use low spinal for vaginal plastics though the anesthesia in this case was entirely satisfactory. The convalescence was disturbed only by a flare-up of cystitis which was noticed after removal of the Foley catheter on the fifth day. Culture was pure colon bacillus and was cleared up very promptly by streptomycin. Her structure supports are perfect.

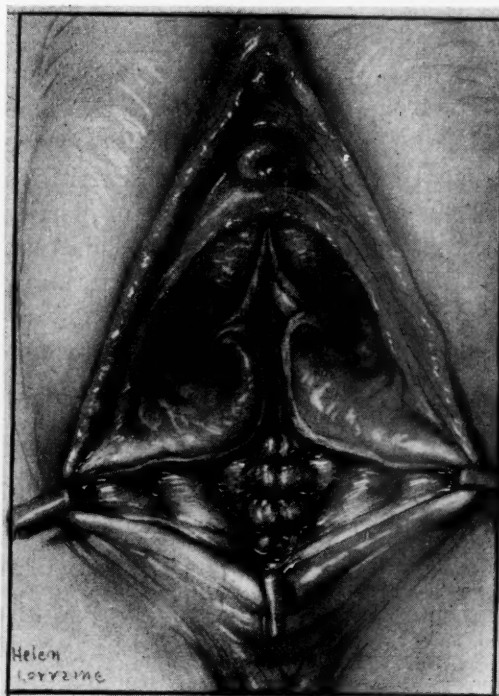


Fig. 10.

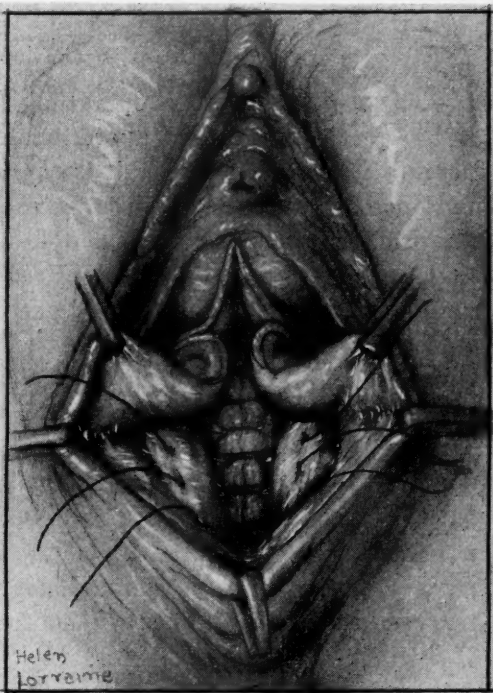


Fig. 11.

Figs. 10 and 11.—Continuation of perineorrhaphy. Sutures of levator ani muscle and fascia.

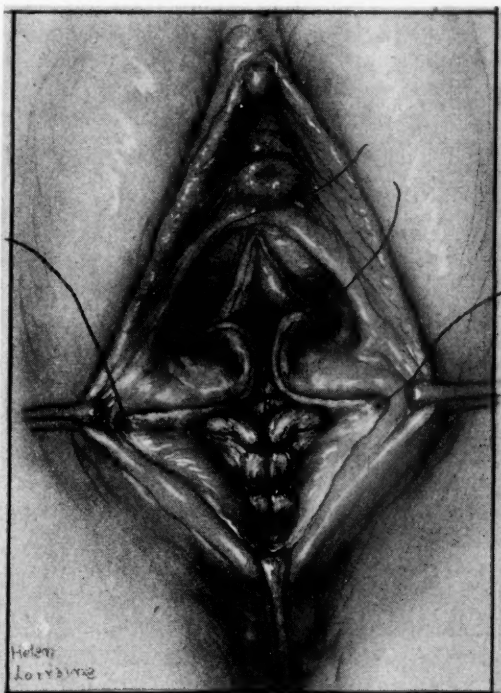


Fig. 12.

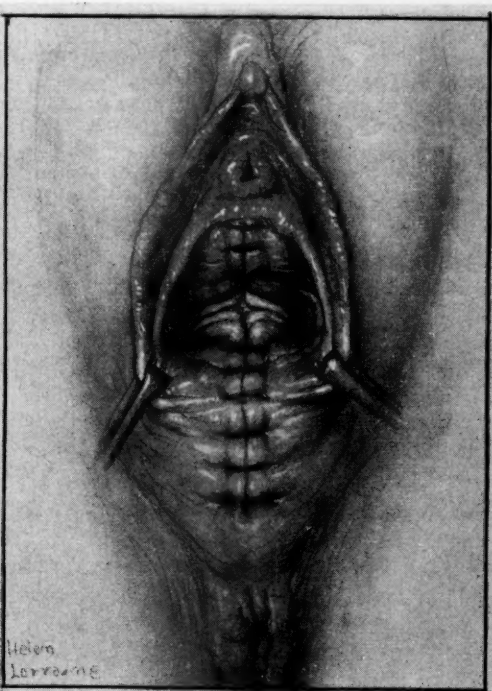


Fig. 13.

Fig. 12.—(a) Perineorrhaphy (continued). "Crown Stitch of Emmet"; additional sutures in perineal fascia as needed. (b) Approximation of vaginal mucosa with interrupted sutures.

Fig. 13.—Mucosal closure complete.

### Discussion

The usefulness of this operation is limited, these limitations being the same as those of any Le Fort operation, in that no provision is made for future marital life, and altogether it is confined to a small group. During the three and one-half years in which these cases were seen, we did 262 vaginal plastics for prolapse, nearly all associated with cystocele and rectocele. This plan has the advantage of being entirely vaginal procedure and is remarkably simple for anyone who is accustomed to doing vaginal plastics. The time required is very short. It eliminates the need for abdominal operation which is undesirable for this particular group, as they do not stand vaginal plastics combined with abdominal operations too well. The second case which I have described would have been entirely unsuitable for any kind of abdominal operation, and very likely no method of suturing the vaginal structures would have been sufficient alone. It seems possible that this procedure might well be used in any case selected for a Le Fort operation as the vaginal plastic is a part of it and offers the advantages of real support. The group suitable for this operation is small but the need for relief is very great.

### Summary

1. A method of repair of inversion of the vaginal tract is described.
2. This method consists of a modified anterior and posterior vaginal plastic combined with a modified Le Fort operation.
3. Two cases are reported, which have been most satisfactory.

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605 MEDICAL ARTS BUILDING



## SIMPLIFIED METHOD OF FETAL ROENTGENCEPHALOMETRY\*

### Results Checked in 482 Cases

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ACCORDING to Clifford,<sup>1</sup> "Hirsch<sup>2</sup> has given a concise review of the various attempts to utilize the x-ray for pelymetry. He points out that five general methods were developed many years ago and all modern methods are, in fact, minor adaptations of these fundamental techniques:

1. *Comparative methods* in which the exposure of the pelvis in the living is compared with a normal specimen taken under identical conditions.

2. *Teleroentgenographic methods* in which the x-ray target is placed far enough from the object to obtain parallel rays and eliminate distortion.

3. *Frame methods*, first suggested by Fabre and Fauchet in 1899, in which a metal frame with its borders notched at centimeter intervals is placed around the patient's pelvis in the plane of the diameter to be measured. The popular Thoms technique is based upon this method except that after the first x-ray the patient is removed from the table and a lead plate perforated at centimeter intervals is placed in the plane to be measured and a second flash exposure made.

4. *Triangulation methods* in which two exposures are made on the same film or on two separate films that are later superimposed. When the x-rays are taken, the shift of the target is a known distance and the target-film distance is also known. "The two shadows of the point in the body are connected and the location of the point above the plate surface may be estimated by a mathematical formula or by a phantom with strings, utilizing the target displacement and the shadow displacement distance as known factors."

This is the principle of the technique first used by Levy and Thumin and by MacKenzie-Davidson in 1898. The methods of Chamberlain and Newell (1912) and Johnson (1927) are recent examples.

5. *Stereoscopic methods* "in which stereoscopic exposures are made and viewed in the regular way. By the use of an illuminated ruler or movable metallic points, placed directly in the phantom image, the pelvis may be accurately measured. . . . It is thus apparent that most of the methods reported in the last few years have been but modifications of the original principles laid down by Varnier, Albert, Fabre, and MacKenzie-Davidson."

Thoms,<sup>3</sup> in 1930, presented a study upon 149 infants x-rayed before birth, with the use of a modification of his grid method in which the perforated lead plate was subsequently inserted at the level of the fetal head as determined by palpation. The second exposure then added the centimeter-spaced dots on the film, not on the plane of the pelvic inlet, but in that of the image of the fetal head. Our method is a modification of that of Thoms and somewhat similar to one by Jarcho<sup>4</sup> which he presented in 1931.

Walton,<sup>5, 6</sup> in 1931, using his false centimeter chart and two films exposed, one horizontally and one vertically, was able to measure the fetal head accurately when there was no intervening fetal movement.

In a classic paper in 1934, Clifford,<sup>7</sup> by a stereoroentgenographic method, was able to predict the size of the fetal head in utero to within 0.3 cm. in 97

\*Read at the Tenth Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists, Augusta, Ga., Feb. 12 to 14, 1948.

per cent of a relatively large series of cases in which there was no head movement interposed between film exposure. In almost 30 per cent of all cases, the movement of the head precluded scientific measurement. His would seem to be an ideal method if the two films could be exposed simultaneously, or almost so.

Ball and Marchbanks,<sup>8</sup> in 1935, reported a teleroentgenographic process by which the volume of the pelvic cavity calculated from the anteroposterior diameter of the inlet and the interischial spine diameter is compared to the volume of the fetal head calculated from the mean circumference of the fetal cranium. They reported sixty cases in which the circumference of the fetal head was exact to within 1 cm. in 85 per cent and to within 2 cm. in the remainder. The weight of the fetus was predicted to within 8 ounces in 85 per cent and to within one pound in the remaining 15 per cent.

Fray and Pommerenke,<sup>9</sup> in 1939, presented an ingenious stereoroentgenographic procedure by which a single film is exposed simultaneously by two stationary x-ray tubes, separated from each other by a constant interfocal distance. This eliminated the chief source of error in all double exposure processes, to wit, the movement of the fetus between exposures. They showed that this was very precise in measuring a steel rod, but they had employed it to a limited extent in fetal cephalometry where the variations in rotation of the head presented some difficulties.

In 1940, Thoms and Godfried<sup>10</sup> measured and plotted the suboccipitobregmatic circumference in seventy newborn infants. They showed that this circumference was ovate in shape with the occipital half narrowed and the bregmatic half broadened. In no case illustrated, was there a radius deviation of more than 0.5 cm. and a clinical study shows that by moulding, in any instance, it may become circular.

Guerriero, Arnell and Irwin,<sup>11</sup> in 1940, made a study of 503 labors in which the Ball volumetric method of x-ray had been employed. They concluded that "in 38 breech presentations, the correlation between the radiologic findings and the clinical course of labor was not sufficiently close to establish the method as of any great prognostic value." They found it more reliable in cephalic presentations.

In 1941, an excellent critical review of all of the previous work was made by Dippel and Delfs.<sup>12</sup> They stated that most of the popularly employed methods result in an accuracy sufficient for clinical purposes, but that, to be scientifically exact, one must resort to the more complicated ones. They justly criticize isometric grid methods in that correct placement of the grid is necessary and may, in certain cases, be impossible. They favored the Hodge triangulation method as being more accurate. As in all double exposure methods, the fetal head may move between exposures.

Cave,<sup>13</sup> in 1943, reported a new triangulation method of double exposure on separate films with the position of the patient and cassette identical in each, but with the tube distance varied.

Kendig,<sup>14</sup> in 1946, devised formulas and tables for facilitating pelvic and fetal head mensuration from stereoscopic films.

In labor, the mechanical problem lies not only in a correct knowledge of the pelvic cavity in question, but also of the size and presentation of the fetus. The problem for solution is simply that of propulsion of a bullet-shaped object, the fetal head, through the roughly curved cavity of the maternal pelvis, the latter of which has two dimensions of marked importance: first, the anteroposterior diameter of the inlet, and second, the transverse diameter of the mid-pelvis or the distance between the ischial spines. Some authors have also im-

plicated the sacral contour, but in many thousands of deliveries studied, not once has this factor been demonstrated in any case of dystocia as the most important defect.

The concept of the fetal head must be clearly defined. In brief, the head is essentially cylindrical. One end of the cylinder is the face and the opposite end is the occiput with the greatest circumference embracing the biparietal and suboccipitobregmatic diameters. The head is attached to the fetal body by the cervical spine which acts as a fulcrum applied to one side of the cylinder and nearer the occipital end. This arrangement has a tendency to compel the head to traverse the pelvic cavity as occipital presentation. Since in almost all cases the fetal head goes through the pelvic cavity with one end of the cylinder presenting, it is necessary to know only the diameter of the cylinder and this is obtainable by ascertaining either the biparietal or the suboccipitobregmatic diameter, since they are, or can be made by moulding, essentially identical. The knowledge of the length of the head (frontooccipital diameter) is of no practical value in dystocia. Only in brow presentations does the head present with the cylinder sideways, so to speak, and these are very rare, probably not any more often than one in two or three thousand labors. Furthermore, they are indisputably diagnosed by the lateral soft tissue film and when diagnosed, their special management is then in order.

*Fetal Head Sizes.*—A review of a large number of term newborn heads measured soon after birth demonstrated that they tend to range mainly from 8 to 10½ cm. in diameter, biparietal or suboccipitobregmatic. Under certain circumstances, the biparietal diameter is the greater, under others the suboccipitobregmatic is greater, but these two diameters seldom vary more than one centimeter from each other. The variation is almost always due to head moulding in labor or to lack of it. A narrow midpelvis with a long duration of occiput transverse presentation tends to produce a fetal head with shortened suboccipitobregmatic diameter. A contracted platypelloid inlet with a long first stage of labor will shorten, by moulding, the diameter of the head, which lies between the symphysis pubis and the promontory. This may be either the biparietal or the suboccipitobregmatic, depending upon the presentation at the time. These observations, noted time and again, have been made over a period of a decade in many thousands of labors, exact records of which are available, as well as the measurements of the pelvic cavities from which they came.

*Technique of This Study.*—The isometric method here used consisted of a single addition to the commonly employed lateral soft tissue technique reported by Snow and Powell,<sup>15</sup> and Dippel and Brown.<sup>16</sup> This addition is that of attaching over the fetal head and as near it as possible a 10 cm. lead scale strapped over the mother's abdomen. It is necessary that this scale lie in a longitudinal plane on an elevation as near the center of the fetal head as possible. When the film is exposed, the scale image then may be used to measure by calipers the diameter of the fetal head in the plane of the biparietal or suboccipitobregmatic diameter, whichever is obtainable at the time. In breech presentation, the scale is placed over the upper portion of the uterus and on a level with the palpable fetal head. The predictable error of the method, if the technique is as exact as possible by a trained technician, is not greater than 5 per cent plus or minus, i.e., 0.5 centimeter. Let it here be stated that the object is for practical aid in prognosticating the course of the labor in question and that it cannot compete with more exacting, but more cumbersome and more costly

triangulation methods. Furthermore, 5 per cent error is no more than that which occurs among a group of physicians who may measure the same newborn head by devices in common usage. A test of its practical value has been that,

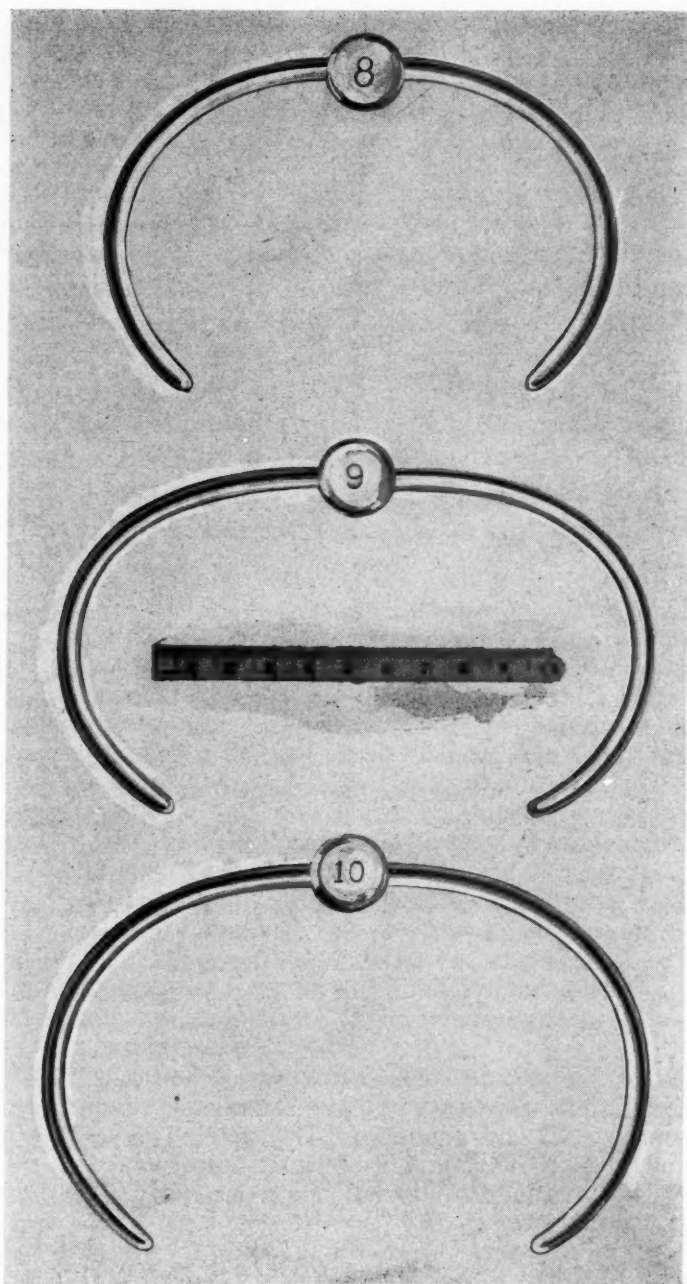


Fig. 1.—Metal gauges to facilitate the measurement of the biparietal and suboccipitobregmatic diameters of the newborn infant's head.

during the seven years of its routine employment in all doubtful labors, the operative delivery incidence has been reduced to approximately one per cent, including forceps and cesarean section. Ninety-nine per cent have delivered



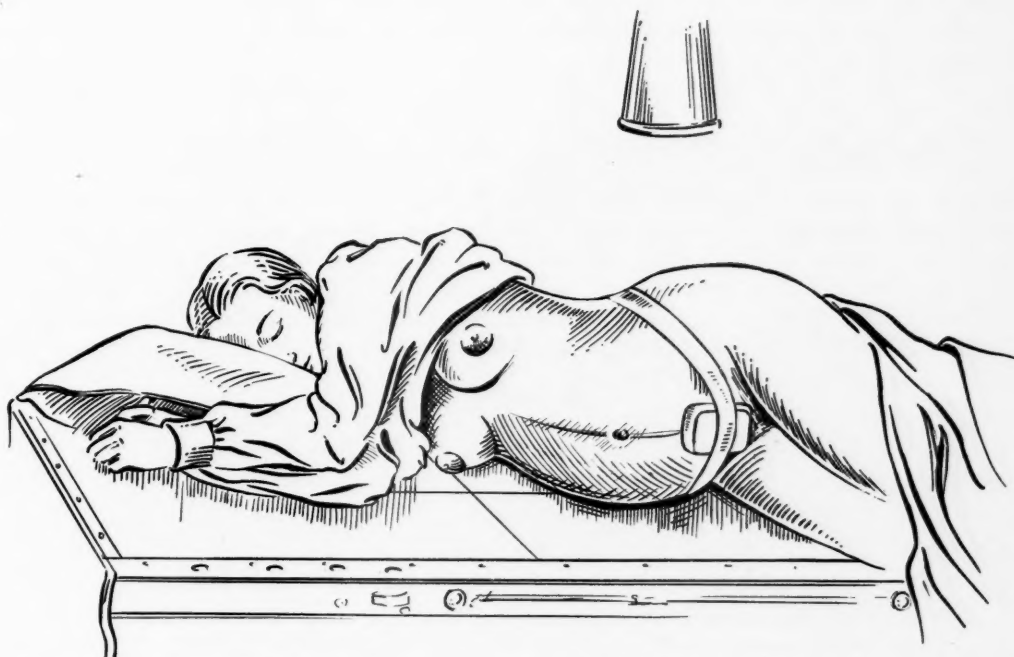


Fig. 2.—Ten centimeter lead gauge strapped over the mother's abdomen and on a level with the greatest diameter of the fetal head at the time of the lateral soft tissue film exposure.

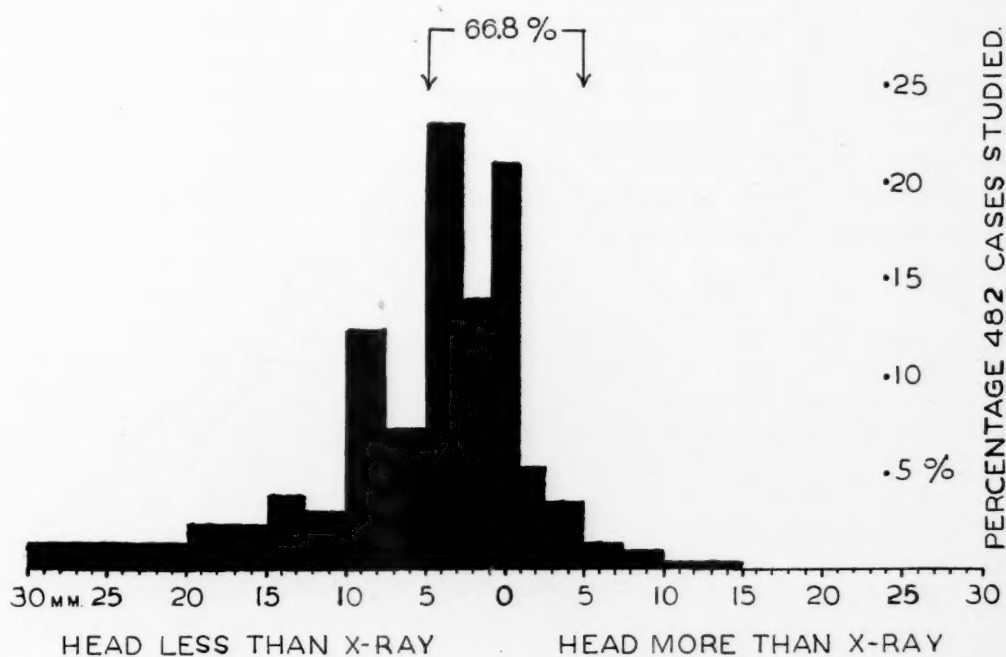


Fig. 3.—Chart showing the degree of accuracy or error in determining by x-ray the biparietal or suboccipitobregmatic diameter of the fetal head in 482 cases investigated.

vaginally, spontaneously, the only aid having been episiotomy and, rarely, Kristeller expression. The fetal and maternal morbidity and mortality have consequently been at a minimum.

In this series of 482 cases, in 321, or 66.7 per cent, the x-ray measurement was within 0.5 cm. of the actual size of the fetal head. In 427 cases, or 88.7 per cent, the x-ray measurement was within 1 cm. of the true size of the fetal head. In all cases with an error of more than 1 cm., the error occurred in taking the x-ray exposure. The centimeter marker must be placed over the fetal head and in the longitudinal plane, if the correct measurement is to be made; in many of our series, the marker was placed by inexperienced technicians who did not understand the principles involved. Almost without exception, if the marker is placed by experienced personnel, the x-ray measurement will be within 5 mm. of the actual measurement.

### Discussion

At the present time, there are several methods of x-ray pelvimetry that quickly reveal the exact size and contour of the pelvic cavity. The ideal is to have such knowledge of the pelvis of every obstetric patient. However, unless one knows the size of the crucial diameters of the fetal head in question, the mechanics of obstetrics is still largely guesswork, as it has been in the past.

Because of the growing popularity of the lateral soft tissue technique in determining the condition of the fetus and the placenta, it would be desirable, in addition, to obtain measurement of the fetal head. This technique makes it possible, but until there is more exact localization of the measuring scale than has been demonstrated here, there can be little reliance upon the prognosis of labor in many of the cases. The study revealed that where due care was taken in placing the marking scale at the level of the fetal head and correct placement of the patient, the error may be kept at 5 per cent. The technique in every case (and this was not always observed in this study) must be supervised preferably by the obstetrician in order to locate exactly the fetal head for application of the isometric scale. Grotesque errors will occur if reliance is placed upon the work of unsupervised technicians.

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## THE USE OF CRYSTALLINE PENICILLIN G IN THE TREATMENT OF SYPHILIS IN PREGNANCY\*†

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PREVIOUS reports on the use of penicillin in the treatment of syphilis in pregnancy indicate that this drug is of considerable value and is more effective than arsenical therapy in the prevention of congenital syphilis.<sup>1-4</sup> In the early studies, amorphous penicillin was used in doses ranging from 600,000 to 2.4 million units. This report presents the results obtained with larger doses, 4.8 million units, of a purer form of penicillin, crystalline penicillin G.

### Case Material and Procedures

The patients in this study consisted of 39 pregnant women with early syphilis. The diagnoses of these patients at the time of treatment were as follows:

Seropositive primary syphilis	2
Secondary syphilis	25
Recurrent syphilis	2
Early latent syphilis	10

None of the patients had had treatment for syphilis except for the two cases with recurrent secondary manifestations. These two had failed to respond to previous penicillin or arsenic-bismuth therapy and developed evidence of relapse during pregnancy. This recurrence of infection was manifested either by a rise in the quantitative serologic test or by a return of the cutaneous lesions. The duration of the infection in the ten patients with early latent syphilis was less than four years and was established by a record of a negative serologic test within that time. Seven of the ten patients were known to have had the infection for less than two years at the time of treatment; two, less than three years; and one less than four years. Thirty-six of the patients were Negro, and three were white.

Each of the patients was treated with a total dose of 4.8 million units of crystalline penicillin G. This was given in doses of 80,000 units every three hours for 60 injections in 7½ days. No additional therapy was administered. After completion of treatment all patients were instructed to return at monthly intervals for quantitative serologic tests and physical examination.

Serologic tests for syphilis were taken on both mother and child at delivery, at monthly intervals thereafter for six months, and then every two or

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three months. Careful physical examination of the child was performed at birth and roentgenographic examination of the long bones was made. Roentgenographic studies were repeated whenever indicated by clinical or serologic findings.

The majority of the patients in this study were treated late in the course of pregnancy. Twenty were treated between the sixteenth and thirty-second weeks of pregnancy; fourteen, after the thirty-second week; while only five began their treatment before the sixteenth week.

Since this study began in July, 1946, the period of observation of the patients has been relatively short. One patient developed evidence of relapse three months following treatment. Three patients have been observed for six to eleven months, twenty-seven for twelve to twenty-three months, and the remaining eight patients for twenty-four months or longer. All of the infants have been observed for at least four months after delivery.

### Results

*Response in the Mother.*—Thirty-four of the 39 patients treated for syphilis in pregnancy have obtained a satisfactory clinical and serologic response. The syphilitic lesions disappeared promptly in these patients and no evidence of recurrence has been noted. Thirty-two of them now have a negative serologic test. In the remaining two patients there has been a continuous decrease in titer since the beginning of treatment. With continued observation, the serologic tests of these patients are expected to become negative.

Five patients have developed evidence of treatment failure following penicillin therapy. Three of these five cases showed a rise in the quantitative test for syphilis after delivery. Their children are not infected. The two remaining patients developed serologic evidence of relapse a few weeks prior to delivery, but one of their children appears to have escaped infection. (These patients were not retreated prior to delivery because the rise in quantitative titer did not become significant until parturition.)

*Effect of Treatment Upon the Infant.*—Thirty-two of the 39 pregnancies have resulted in normal, living, nonsyphilitic infants. Three children were born with syphilis and the infants of four other pregnancies did not live. Of the 32 living and nonsyphilitic children, one child has been observed for four months following delivery, the remaining thirty-one for six months or longer.

The serologic test for syphilis in fifteen of the thirty-two normal children was positive at birth, but became negative in several weeks without treatment. The positive tests were probably caused by a transfer of reagin from the mother, since the maternal serologic tests in these cases were also positive at delivery. Positive serologic reactions in the mother at delivery occurred in 31 of the 39 patients. This was to be expected, since the majority of patients did not receive treatment until late in pregnancy. The titer, however, was decreasing in almost every case.

*Occurrence of Syphilis in Infants.*—Two of the three children born with syphilis were delivered while their mothers were receiving treatment. In one instance the child was born on the first day of treatment after its mother had received only 240,000 units of penicillin. This patient had entered the hospital in the eighth month of pregnancy because of rupture of the membranes. She was found to have secondary syphilis, and penicillin therapy was started. Labor began four hours later. The child was normal at birth but had a serologic reaction of 20 Kahn units. Three months later the titer had risen to 80 Kahn units, and treatment was begun. The other syphilitic baby was born on the



fourth day of treatment after the mother had received 2.24 million units of penicillin for secondary syphilis. This child was a premature infant, weighing 2,100 Gm., and had a positive serologic test of 1,280 Kahn units. Roentgenographic examination revealed rarefaction of the long bones proximal to the epiphyses, and the diagnosis of syphilis was made.

The presence of syphilis in these two infants was to be expected, since the course of therapy had not been completed. If the mothers had received the entire amount of penicillin before delivery, the treatment might have been successful. One such instance appeared in this series.

This was a patient with early latent syphilis who delivered a 2,500 Gm. infant on the seventh day of treatment after having received four million units of penicillin. The serologic test for syphilis of the mother was 40 Kahn units while that of the child at birth was 80 Kahn units. Roentgenograms of the infant showed evidence of syphilis of the long bones. This child was not given further therapy and spontaneously developed a negative blood test and healing of the osseous lesions. This, we believe, is evidence that penicillin can effect a cure of the fetus in utero even though it is already infected.

The third child with syphilis was found to have serologic and roentgenographic evidence of the disease at 9 weeks of age. His mother was treated for secondary syphilis at the fourth month of pregnancy, but showed a serologic relapse four days before parturition. She delivered before retreatment could be given.

*Delivery During Treatment.*—The mothers of three of the children described above delivered during penicillin therapy. Two other patients treated in the last eight weeks of pregnancy also went into labor while receiving penicillin.

In one instance, a mother with secondary syphilis delivered a 2,500 Gm. infant after having received only one million units of penicillin. The serologic test of the infant was doubtful at birth but became, and remained, negative without treatment. There was no roentgenographic or clinical evidence of syphilis in this infant.

The second patient had early latent syphilis of one year's duration and went into labor at the conclusion of penicillin therapy. She delivered a 1,390 Gm. macerated still-born infant three hours later. Fetal heart tones and movements had been noted at the onset of treatment, indicating that the infant died during the course of therapy. Roentgenographic studies of the long bones were not obtained. Although the cause of death could not be determined at autopsy because of the severe maceration of the tissues, the infant probably died as a result of syphilitic infection.

There was only one patient who delivered prior to the thirty-second week of gestation. She had a spontaneous abortion which occurred in the fifth month of pregnancy. The patient had typical eclampsia and was receiving penicillin therapy for secondary syphilis.

*Infant Deaths.*—Four fetal or infant deaths occurred in this study. Two of the deaths have been described in the foregoing paragraphs.

The third child died three days after delivery. The mother of this child had received penicillin for secondary syphilis six weeks previously and delivered a full-term infant. The child showed evidence of asphyxia at birth and responded poorly to artificial respiration, oxygen, and coramine. He developed a temperature of 105.6° F. four hours after delivery and was treated for aspiration pneumonia. Despite penicillin therapy, death occurred two days later. The serologic test was positive with 10 Kahn units. The mother's serologic test was 20 Kahn units. Roentgenographic examination of the infant's long bones showed slight periosteal thickening, but no definite evidence of osteochondritis or osteomyelitis. Intrauterine disease had apparently been present, as shown by an arrest of bone growth. This had been followed by new bone formation, and the lesions were in-

terpreted as healing syphilis. Autopsy revealed bronchopneumonia, pulmonary atelectasis, and pulmonary hemorrhages. Histologic examination of the long bones showed osteitis consistent with healing syphilis.

The fourth death was that of a 1,650 Gm. macerated stillborn infant. The mother in this instance had been treated three weeks before delivery for early latent syphilis of less than two years' duration. Fetal movements had been felt four days before the onset of labor. Roentgenographic examination of the long bones of this child showed severe osteochondritis and osteomyelitis, in addition to numerous pathologic fractures. The severe maceration of the tissues prevented satisfactory histologic examination at autopsy. The death of this infant was probably the result of a syphilitic infection which had failed to respond to the treatment given three weeks previously.

### Comment

The results of this study indicate that crystalline penicillin G is of considerable value in the prevention of congenital syphilis, even when given late in pregnancy. All of the patients in this series were in an untreated infectious stage of syphilis, and more than one-third of them began therapy after the thirty-second week of gestation. The effectiveness of penicillin was, therefore, evaluated by the most rigorous circumstances, i.e.: the existence of early untreated syphilis detected late in pregnancy. It has been estimated that approximately 95 per cent of such patients will have congenitally syphilitic children if no treatment is given.<sup>4</sup> In this study only three living children had syphilis, and two of these were delivered before the therapy was completed.

The two stillbirths in this study were probably the result of severe syphilitic infection. It is likely that the infection in these infants had produced such advanced tissue destruction that no form of therapy would have been successful. For this reason treatment with penicillin should be started early in pregnancy if possible.

The abortion which occurred in the fifth month of pregnancy may have been caused by eclampsia. Another death, that of the child which died three days after delivery, was adequately explained at autopsy by the presence of extensive bronchopneumonia.

It is difficult to compare our results with those obtained with arsenical therapy. In most of the reports on the use of arsenicals in prenatal syphilis, no distinction was made regarding the duration of the infection in the mother or the amount of previous treatment. Despite the lack of accurate comparative data, there is no doubt that penicillin is more effective than arsenical therapy in this condition. It has been estimated that arsenical therapy of patients similar to ours would result in about 15 per cent to 20 per cent of the children having congenital syphilis.<sup>1, 5</sup>

The reports of other workers using amorphous penicillin showed approximately 6 per cent fetal deaths probably not related to syphilis, and 4 per cent syphilitic infants.<sup>4</sup> These results were somewhat superior to those observed in the present study. It should be emphasized, however, that a large proportion (35.9 per cent) of our patients were treated in the last eight weeks of pregnancy.

Five (12.8 per cent) of the 39 mothers in this series developed evidence of treatment failure. This relapse rate is comparable to that generally obtained with penicillin in early syphilis after a similar period of follow-up observation. It must be emphasized that a quantitative serologic test for syphilis should be taken at frequent and regular intervals following therapy. This is the only way that relapses in pregnancy can be detected sufficiently early to prevent congenital syphilis. A positive serologic test following therapy or at delivery

does not in itself indicate treatment failure, provided the titer is decreasing. Retreatment in pregnancy, preferably with larger amounts of penicillin, is indicated if the patient develops serologic or clinical relapse.

The fact that six of the patients in this series began premature labor during the course of treatment is worthy of comment. Two patients had conditions other than penicillin therapy which could well explain the onset of labor. The membranes had already ruptured in one case, while the other aborted spontaneously after eclampsia. The remaining four cases were treated in the last eight weeks of pregnancy and constituted 28.5 per cent of the fourteen patients receiving therapy in this stage of gestation. This high incidence of premature delivery suggests that the onset of labor may have been related to the large doses of penicillin used in this study. Other workers have also noted the onset of labor during penicillin therapy and have attributed it to therapeutic shock.<sup>4, 6</sup>

The patient with eclampsia has had a subsequent pregnancy and delivered a normal infant despite the fact that she continued to have a positive serologic test of low titer (4 Kahn units) and received no additional therapy. Five other patients have had subsequent pregnancies and have delivered normal children without further therapy. Similar cases have been recorded in the literature; and it is apparent that treatment with penicillin may protect the mother and baby in subsequent pregnancies.

### Summary

Thirty-nine pregnant women with early syphilis were treated with 4.8 million units of crystalline penicillin G and followed for at least four months after delivery. Treatment was started after the thirty-second week of pregnancy in more than one-third of the patients.

Six patients went into premature labor during penicillin therapy and two of their children were born with congenital syphilis. One patient developed a serologic relapse prior to parturition and delivered a syphilitic child. There were four infant deaths, two of which were probably caused by syphilis. The remaining 32 children are now living and nonsyphilitic.

Five (12.8 per cent) of the 39 mothers have shown evidence of relapse of their syphilitic infection.

The results obtained in this series of patients with early infectious syphilis treated in the late stage of pregnancy indicate that crystalline penicillin G is an effective therapeutic agent in prenatal syphilis.

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## OPERATIVE OBSTETRICS\*

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**T**HINKING in terms of our present obstetrical practice, it is difficult for us to realize that crude and often brutal methods were in use only a century ago. Very little progress had been made since Ambroise Paré rediscovered internal podalic version and Chamberlen the obstetric forceps. For the most part, the care of parturient women was in the hands of more or less ignorant midwives and a physician was rarely called until the woman with severe dystocia was exhausted from the pangs of a blocked labor. Craniotomy was a rather common operation and cesarean section was limited to the unfortunate few whose pelvis were too small to permit a destructive removal of the fetus.

Holmes and Semmelweis had recognized that puerperal fever resulted from contamination, but years passed before the development of the new science of bacteriology made possible a definite proof of its infectiousness. Rokitansky, in 1864, had observed microorganisms in lochial discharges and a year later the streptococcus was identified by Myerh. Two years later Coze and Feltz found microorganisms in the blood of a woman who had puerperal fever. However, it was not until 1879 that Pasteur presented his thesis on "Septicémie Puerperale," reciting his laboratory observations on cultures made from the lochial discharges, the blood, and the peritoneal cavities of women who died from puerperal fever. Since in all of these he obtained pure cultures of streptococcus, he concluded that these organisms were "probably the determinants of that very dangerous disease." Thus Pasteur completed the series of observations begun by White, Gordon, Holmes, and Semmelweis and thereby paved the way for the antiseptic methods introduced by Lister. But many more years passed before modern aseptic methods made possible the obstetric surgery of today.

My own practice of obstetrics began a third of a century ago and it ended with a low-forceps delivery the day before Christmas, 1947. During these years I have witnessed many changes. My preceptor, J. Clarence Webster, in his time was called a radical cesarean sectionist by Dr. DeLee. At the time of his retirement in 1919 he had performed 150 classical and Porro operations with two maternal deaths. During the years after the introduction of the low cervical operation, Dr. DeLee performed several times that number of cesarean sections. Today Dr. Webster probably would be considered ultra-conservative.

The simple and very valuable operation of episiotomy rarely was used prior to 1915, when its value was demonstrated by Brooke Anspach. In my early practice we boasted of our low incidence of forceps deliveries. As late as 1928, I visited one European clinic where, with a yearly average of about

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1,800 deliveries, they reported only 10 or 11 forceps deliveries and some 50 cesarean sections each year. When, in 1920, Dr. DeLee presented his paper on "The Prophylactic Forceps Operation," he was generally condemned by the members of the American Gynecological Society. Today we realize that a low-forceps delivery may be much safer for both mother and infant than a more prolonged labor with an excessive use of Kristeller pressure in the effort to record another so-called normal delivery.

About 1861, Simpson stated that induction of premature labor a century earlier was "perhaps the greatest improvement that has ever been made in the practice of midwifery." However, the greatly reduced risk of the cesarean operation has materially lessened the incidence of premature induction of labor several weeks before term. Induction of labor at term, on the other hand, is now being advised by a few obstetricians and they have demonstrated that, properly employed, it is a safe and possibly a conservative procedure. Induction at term must not be confused with induction of premature labor. If the cervix is patulous and the head fixed in the pelvis, labor may be expected to follow shortly after the membranes are ruptured, and available data indicate that the duration of labor on the average is shortened. If the head is not engaged or the cervix is rigid with no effacement, artificial induction of labor rarely is justified.

Craniotomy a century ago was a rather common operation. Most of us will agree that it is no longer proper to consider it unless the fetus is very abnormal or already dead. The extraperitoneal cesarean section, as developed by Waters, or the more recent modification of Norton, is probably less dangerous for the mother than a craniotomy.

About 1920, Potter of Buffalo reported before the Philadelphia Obstetrical Society 1,113 labors with 920 versions and 80 cesarean sections. However, his immediate fetal mortality was 6.7 per cent and those who tried his version soon realized that it was not a proper substitute for normal labor. Nevertheless, he has added to the technique of a valuable operation which has definite indications and is at times the only proper procedure.

Twilight Sleep appeared just as I was starting my private practice of obstetrics. The group with which I worked in Chicago was much interested in the development of nitrous-oxide-oxygen analgesia and eventually I adopted the best parts of both methods, using heroin with the hyoscine, rather than morphine, and limiting the gas to the second stage of labor. More recently I have used Demerol with hyoscine since heroin is no longer available. In 1920, while discussing a paper on the use of ether in obstetrics I made the following statement: "Recently I have been using nitrous-oxide-oxygen analgesia intermittently for both mid- and low-forceps deliveries as well as in normal labor. The nitrous oxide-oxygen is given to a deep analgesia or light anesthesia while the forceps is applied. The mask is then removed, and thereafter the gas is given intermittently as in normal labor. The patient is instructed to bear down during contractions while gentle traction is made on the forceps. For primiparas, I do a primary posterior episiotomy. There is usually an easy delivery with a minimum of traction pressure on the head." After using this plan for some thirty years, I still believe it is safer for the fetus than use of the greater traction that is required when the woman is deeply anesthetized and unable to assist.

Many years ago, I began making yearly checks on my obstetrical work so that I could compare my results with those reported by others. In 1926, a survey of my first 500 deliveries in Milwaukee was presented before the Chicago Gynecological Society. Later, in 1941, a complete report on the obstetrical part of my private practice in Milwaukee was published in the

*Western Journal of Surgery, Gynecology and Obstetrics.* These papers indicate gradually changing views regarding the management of pregnancy and labor. Data covering my 11 years in Wilmington have now been added making it possible to cover a twenty-eight-year period.

Spontaneous delivery, frequently after a mediolateral episiotomy, occurred in 1,100 cases; there were 595 low forceps, 461 midforceps and 28 high applications. Cesarean sections were performed 125 times, with 64 classical, 48 low cervical and 13 Porro operations. Six patients had vaginal hysterotomies and forceps deliveries. Version and extraction were employed 14 times and there were 99 breech presentations. The Piper forceps was applied to the aftercoming head in 30 deliveries. Out of a total of 2,456 babies, there were 26 sets of twins and one of triplets. Thirty-one babies were still-born and 36 others died during the first month of life, a fetal loss of 2.71 per cent. Five women died, just over 2 per 1,000 women.

Prematurity, under seven months, was the major cause of death for 20 of the babies who died the first month. Three babies died during an outbreak of "diarrhea of the newborn." Four had very serious heart defects proved by autopsy. Hemorrhagic disease of the newborn killed two. Three had marked atelectasis proved by x-ray or autopsy. Erysipelas of the penis following circumcision killed one. Erythroblastosis was responsible for one. One developed pyelitis and died on the eighteenth day. Another was lost through virus pneumonia which developed after going home.

Fifteen of the stillborn babies were macerated, having died before the onset of labor. Erythroblastosis caused a few of these deaths. True knots of the cord and extreme twisting caused others. None resulted from syphilis; in fact, only two of my patients ever indicated any evidence of this condition. Of the sixteen babies lost during labor, 5 were monsters (anencephalic); three died as a result of premature separation of the placenta; one, a five and one-half month fetus, died during labor while the mother was unconscious with a severe nephritic toxemia; seven normal babies were lost as a result of prolonged tests of labor prior to operative interference, or as a result of pressure on the cord during an easy normal labor. The loss of these seven babies led to more frequent checking of the fetal heart rate and earlier operative interference when changes in the rate suggested impending asphyxia. In one case, partial premature separation of the placenta made it necessary to accomplish a rapid delivery by classical cesarean section. Thirty minutes of artificial respiration were required for resuscitation. In this case the baby developed a beautiful body but was a total idiot. We now have definite experimental proof as well as clinical that fetal asphyxia rapidly destroys brain cells and every effort must be made to avoid it during labor.

Five mothers were lost. One died in convulsions some twelve hours after her delivery; one had an influenzal pneumonia and one developed a paralytic ileus with an unrecognized appendicitis following delivery by cesarean section a month or more after term. Autopsies were obtained on these three. More recently two more mothers died, one from a pulmonary embolus within an hour after delivery; the other with a thyroid crisis and heart failure. Autopsies were refused in these cases.

Approximately 5 per cent (125) of my patients were delivered by cesarean section. The one woman who died from ileus and appendicitis had been delivered through the natural passages four times previously but this time the baby which weighed just under 11 pounds was too large. Several of the other women who required cesarean section had been delivered by me one or more times before they developed a baby that was too large for their

natural passages. Three cesarean sections performed in 1945 and 1946 were on women whose pelves were ample for babies of average size; one had been delivered twice by forceps and one had a record of four normal labors; one was a primipara with an oversized baby.

A cesarean section still is far more dangerous than delivery through the natural passages. Moreover, the mortality associated with a single cesarean does not tell the entire story, for risks multiply with each succeeding pregnancy. I sometimes wonder if we are entirely justified in discontinuing premature induction of labor when there is evidence that the baby will be too large if the pregnancy continues. I feel certain that in the future fewer women will be permitted to continue very long beyond term.

Breech deliveries are somewhat more dangerous for the fetus. One of the babies that I delivered easily, without the use of forceps on the aftercoming head, is somewhat spastic, suggesting a possible birth injury, but a congenital defect is equally probable. One of the most serious objections to version and extraction is the increased danger to the baby from the breech birth. I have rarely attempted external version on any of my private patients since such a high percentage will convert spontaneously during the last month of pregnancy. Furthermore, I always recall that one of my former patients lost a baby as a result of a forcible conversion under anesthesia, while under the care of one of my friends who routinely tries to convert all breech cases to vertex.

High forceps is no longer favored except in an occasional multiparous woman where there is no evidence of disproportion. I have reported a rather high percentage of midforceps deliveries since I have so classified practically all cases requiring rotation from the transverse or posterior position even though the caput may at times make the head appear to have reached the perineum. All statistics indicate that an outlet forceps delivery fairly early in the second stage is safest for the infant since it shortens the labor, thereby lessening the damage from edema of the brain and the risks of asphyxia from pressure on the cord.

There is no reliable data on fetal mortality 100 years ago, but we know that it was very high during the first year of life. Although it is evident that the members of this group will have a gross loss of around 3 per cent, counting stillbirths and deaths during the first month of life, most hospitals are reporting a loss of about 5 or 6 per cent of the babies born in the institution. It seems obvious that statistical information should be required on all hospital deliveries and those physicians whose records show abnormally high infant or maternal mortality should be definitely restricted. Every man's work should be checked separately and judged on his results.

One hundred years have now passed since James Y. Simpson began the administration of ether and chloroform during the painful stage of labor. Obstetric progress has been slow, so slow that at times no progress could be noted for long periods. It was over 100 years after Dr. Physick and Professor Horner had demonstrated in the dissecting room the possibility of an extraperitoneal cesarean section that Waters developed his operation. The year I graduated from Rush Medical College (1909), Dr. A. L. Smith of Montreal read a paper before the American Gynecological Society, entitled, "We Are No Longer Justified in Sterilizing Every Woman Who Has a Cesarean Section." Today we can state that the extraperitoneal cesarean operation has removed the earlier reasons for craniotomy or a Porro section in the contaminated case. However, contamination never was a proper indication for the Porro cesarean hysterectomy since it could not be performed without infecting the peritoneal cavity.

Great progress has been made within recent years and both infant and maternal mortalities have dropped materially since 1940. It is my belief that the next great change in obstetric practice will be in the development of groups who will work as units. Those who have tried this plan have found that it makes possible an improved service to the patients and greatly lessens the physical strain on the men in the group. Obstetricians working in such groups will be able to give better service to the women in labor as well as in the office during prenatal care, since a continuity of service is possible. One man would be on duty at the hospital all of the time and patients in labor would be watched more carefully than at present. Too much is now being left to the inexperienced judgment of nurses and interns. After being up all or most of a night, a doctor would be assured adequate rest the next night. Patients would no longer need to change office appointments because the doctor was called to the hospital. One of the group would be on duty in the office during the entire day.

The young obstetricians who are being certified by the American Board today have had opportunities denied to those of us who began specialty training thirty and forty years ago. We rightfully expect from them continued progress toward making pregnancy and labor still more safe for both mother and baby.



## Original Communications

### PLASMA VOLUME AND EXTRAVASCULAR FLUID VOLUME DURING PREGNANCY AND THE PUERPERIUM\*†

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#### Introduction

THE purpose of this study was to investigate the changes that occur during normal pregnancy in the circulating red-cell mass and plasma and extravascular fluid volumes. It was felt that determining the normal relationship between these three compartments in uncomplicated pregnancy might aid in evaluating changes occurring in abnormal pregnancy.

This report presents results of the simultaneous determinations of plasma volume and extravascular fluid volume. A subsequent paper will give the results of the measurements of the circulating red-cell mass as determined with the radioactive isotope of iron, Fe 55. Another paper will discuss the changes in the capillary bed in pregnancy.

Previous studies of plasma and extracellular fluid volume have been confined to observations of one or the other. To appraise adequately the changes in the vascular and extravascular compartments, simultaneous and frequent determinations on the same patients must be made. In the work published thus far, this has not been done. Dieckman and Wegner<sup>1</sup> in 1934 reported the results of plasma-volume changes in pregnancy as measured with the dye, Congo red. Their finding of a 25 per cent average increase in plasma volume in pregnancy is lower than the values found in subsequent studies.

Thomson et al.<sup>2</sup> in 1938 reported the results of plasma volume determination using the Evans blue dye technique.<sup>3</sup> These investigators found that plasma volume increased progressively and reached a maximum in the ninth lunar month. This value was 65 per cent higher than the "average normal nonpregnant" value. A prelabor plasma-volume decrease was noted and they state that normal nonpregnant levels were reached by the end of the second week in the puerperium.

McLennan<sup>4</sup> has recently published the results of plasma-volume determinations in pregnant patients at term and on the seventh postpartum day. In analyzing his material, this author uses a mean plasma volume determined in

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nonpregnant women to compare with the mean plasma volume of a group of pregnant women. This author points out that the range of plasma volume in pregnancy is greater than in a group of nonpregnant women. Hence, it would appear that the changes in the plasma volume of an individual patient during pregnancy should only be compared with her own nonpregnant level. This volume level, ideally, should be determined in the prepregnant state. However, for obvious reasons this is not feasible. Therefore, a later postpartum determination must suffice for the nonpregnant level. In addition, a prelabor decrease in plasma volume was not noted. This is understandable because, with only one antepartum observation, one would be unable to detect the peak of plasma volume increase.

It is obvious that there is no agreement regarding the degree of increase in plasma volume and the time in gestation when the maximum change is present. The occurrence of a significant prelabor decrease is also in question.

With the exception of Chesley's work,<sup>5,6</sup> extracellular fluid has not been studied during normal pregnancy. Using sodium thiocyanate, he was able to measure the extracellular fluid volume on a large number of pregnant women. Although Chesley's observations were scattered over many patients, a definite trend was noted. He showed that as pregnancy progressed there was an increase in the "available water." Loss of available water in the puerperium was also measured, but because of the interval of time between measurements, he felt that his observations were not particularly valid. In addition, Chesley interpreted certain data obtained on normal pregnant women as suggestive of an intracellular transfer of water to the extracellular spaces.<sup>6</sup>

### Material and Methods

Ten subjects were used in this study and 6 to 12 observations were made on each. It was our desire to study many patients, but a composite study such as this on a larger group of patients would not be practical since the radioactivity determinations alone are time-consuming and expensive. The patients who were used as subjects were healthy multigravida and primigravida women. Their diets were adequate and unrestricted and no medication of any kind was taken during pregnancy or the puerperium. Observations were made at 5- to 6-week intervals throughout pregnancy; the earliest determination on one patient was made 230 days prior to delivery. An attempt was made to have the final prepartum observation as close to the onset of labor as possible and a determination was made during early active unmedicated labor in one case. In the puerperium, volumes were determined at the end of the first week in 5 cases. The last postpartum observations were made on the 26th to the 66th days of the puerperium.

Plasma volume was measured by using the blue dye T-1824. The technique used was that described by Gibson and Evans.<sup>3</sup> In order to answer a previous suggestion that the dye might not be completely mixed and possibly trapped at the placental site,<sup>4</sup> the following procedure was done. A patient with a normal term pregnancy while under spinal anesthesia and prepared for an elective cesarean section, was given 10 mg. of T-1824 and 50 c.c. of whole fresh radioactive red blood cells in the left antecubital vein. Prior to this injection, the left uterine vein had been cannulated with polyethylene tubing. The tip of this tubing was placed as far into the uterus as possible. Simultaneous samples of heparinized whole blood were then withdrawn from the cannulated uterine vein and from the right antecubital vein at 1, 3, 5, and 7 minutes after the injection of the blood and dye. When the

plasma samples were checked photocolorimetrically, the dye concentration in the uterine and arm samples was the same. No difference was found in the radioactivity of the blood samples which were withdrawn simultaneously. It is felt that this is evidence that blood is not trapped at the placental site during its circulation through the uterus in a full term normal pregnancy.

Extracellular fluid was measured by the use of intravenous 5 per cent sodium thiocyanate. Thiocyanate was determined using the method described by Chesley.<sup>7</sup> Serum and urine samples were checked in triplicate. Since the plasma volume is included in the thiocyanate space, extravascular fluid volume could be calculated.

### Procedure

On the morning preceding the test the patients were admitted to the hospital. Following a fat-free lunch, an injection of 5 per cent sodium thiocyanate was given intravenously. Eighteen to twenty hours were allowed for equilibration of the thiocyanate. All of the urine voided during this period was collected. Fluids were not restricted and patients were active about the ward. The next morning, under fasting, basal conditions, 10 mg. of T-1824 and 100 c.c. of whole fresh radioactive blood were given to measure simultaneously plasma volume and the circulating red-cell mass. A serum sample for thiocyanate concentration was taken prior to this injection. Heparinized samples of whole blood were then withdrawn without stasis at ten-minute intervals for fifty minutes. The procedure was then completed exactly as described in previous papers.<sup>3, 5</sup>

### Results

*Plasma Volume.*—The absolute plasma volume values obtained in 10 patients during the course of pregnancy are individually illustrated in Fig. 1. The nonpregnant plasma volume levels were taken as those observed approximately thirty days postpartum. At this time these latter volumes were found to be about 5 per cent of body weight, this percentage being generally accepted as the normal adult value.

Without exception, it will be noted that there was a progressive increase in plasma volume up to approximately 68 to 5 days prior to the onset of labor. This increase in volume ranged from 955 c.c. to 2,015 c.c., with an average increase of 1,366 c.c. In 8 full term pregnancies, there was an average prelabor decrease of the plasma volume of 347 c.c. from its mean maximum value. The plasma volume did not decrease but the prelabor values remained stationary in the other cases. One was a full-term mild pre-eclamptic pregnancy (Case 12) and the other a case of premature labor (Case 5). The plasma volumes observed on the seventh postpartum day were greater than those determined one month after delivery (Table I).

During the course of this study, the determinations on two patients were such as to deserve special mention. In Fig. 1 (Case 5) are shown the changes in plasma volume observed in a patient who delivered prematurely. On the 128th day prior to the estimated date of confinement, the maximum plasma volume was attained. This volume was again observed 80 days prior to the estimated date of confinement which actually preceded the onset of premature labor by 11 days. At this time the patient was delivered of a living infant weighing 2,438 Gm. One wonders whether this lack of change in plasma volume reflects the impending onset of premature labor. Because of the lack of data in previous studies of the plasma volume changes in the early puerperium, several determinations were made during this period on Case 15.

TABLE I. PLASMA AND EXTRAVASCULAR FLUID VOLUME IN PREGNANCY AND THE PUERPERIUM

CASE NO.	PARITY	WEIGHT IN POUNDS	DAY ANTE PARTUM	DAY POST PARTUM	PLASMA C.C.	VOLUME C.C./KG.	LVHCT*	EXTRA-VASCULAR C.C.	FLUID VOLUME C.C./KG.
5	2	134.5	159		2810	46.0	41.4	11,850	194
		140	93		3600	56.5	36.3	14,350	223
		145.5	53		4400	66.5	33.8	15,150	230
		151.5	11		4400	64.0	33.8	15,400	224
6	1			7	3000		30.9	10,400	
		127		66	2730	47.0	36.1	12,600	219
		109.5	172		2800	56.5	39.9	10,050	212
		119	131		3366	62.0	37.7	11,900	220
		128	90		4100	70.5	34.7	12,700	218
		135	49		4160	68.0	32.5	16,300	266
		145.5	3		3460	52.4	35.2	23,200	318
		119		45	2710	50.1	38.2	10,600	196
7	1	100.5	208		2154	47.7	39.2	13,300	293
		105.5	161		2566	54.0	35.3	11,234	304
		109.5	123		3080	61.6	32.2	11,000	220
		119.5	82		3480	64.0	31.1	13,000	239
		114	41		3750	72.0	28.1	14,800	284
		119.5	0		3300	60.7	32.2	15,500	286
		104.5		26	2180	46.2	37.4	9,750	206
		111	132		2800	56.0	37.6	8,230	164
8	2	120	91		3110	57.0	35.6	10,700	231
		124	50		3315	58.8	32.5	11,100	196
		130	8		3060	51.7	35.7	14,000	237
		118.5		7	2640	49.0	35.5	12,100	224
		109.5		33	2360	47.5	38.0	8,650	174
		151.5	148		3973	57.3	35.9	16,100	239
		155	111		4630	65.5	32.3	20,600	280
		157	78		5285	74.0	31.7	14,900	204
11	1	160	39		5425	75.5	29.4	15,600	214
		160	4		4975	68.5	32.5	16,700	228
				7	3500		37.8	16,600	
		150		65	3410	50.0	34.6	15,000	220
		120	215		2440	44.8	37.0	11,000	202
		124.5	180		2714	48.0	35.4	11,750	207
		133.5	138		3110	51.3	34.2	11,600	193
		134.5	90		3515	57.5	31.9	11,000	181
12	1	138.5	53		3410	54.1	33.6	14,500	230
		149.5	8		3710	54.5	32.9	16,800	247
		149	5		3710	54.7	32.9	17,150	253
		120		30	2680	49.2	33.7	11,200	203
		148	200		2930	32.7	39.6	14,200	212
		162	140		3290	44.5	37.5	15,000	204
		169.5	104		3510	45.5	34.4	15,400	200
		165.5	68		4400	58.7	32.5	14,500	194
13	1	178	24		4200	51.7	35.2	25,500	310
		181.5	1		3710	45.0	36.5	20,000	242
		153		30	3080	43.7	38.7	13,900	197
		122	233		2850	51.0	39.6	11,700	210
		126	189		3380	59.0	36.5	11,800	204
		133	147		3720	61.5	34.6	12,700	210
		140	97		3600	57.0	35.0	14,300	224
		145	55		3960	60.0	33.7	12,350	187
15	1	150	18		4000	62.3	33.3	15,400	225
		150	11		3840	60.8	32.0		
				labor	3260		34.1		
				1	2950		36.5		
				3	3340		35.4		
		130		6	3520	59.6	34.4	12,600	213
		122		30	2710	49.0	37.6	12,150	218



TABLE I—CONT'D

CASE NO.	PARITY	WEIGHT IN POUNDS	DAY ANTE PARTUM	DAY POST PARTUM	PLASMA C.C.	VOLUME C.C./KG.	LVHCT*	EXTRA-VASCULAR C.C.	FLUID VOLUME C.C./KG.
16	1	110.5	196		2960	62.0	35.6	11,050	220
		117	161		3290	62.0	34.9	11,500	216
		122.5	120		3420	61.6	34.2	12,680	228
		124.5	78		3525	62.4	32.2	12,400	220
		132	43		3620	60.4	33.5	13,600	225
		137	6		3580	57.5	34.5	15,850	257
		117		45	2665	48.0	37.3	11,650	219
17	2	129.5	200		3580	61.0	36.4	13,900	237
		130	165		3615	61.0	34.1	14,200	240
		139.5	126		4200	66.0	32.3	16,350	254
		148.5	85		4150	65.5	32.3	16,000	238
		151.5	44		4325	63.0	31.5	18,200	270
		155	16		4600	65.0	29.8	20,600	300
		157	4		4560	64.0	28.6	20,500	292
				7	3580		21.2	16,400	229
				33	3200	58.0	35.0	13,200	215
		136							

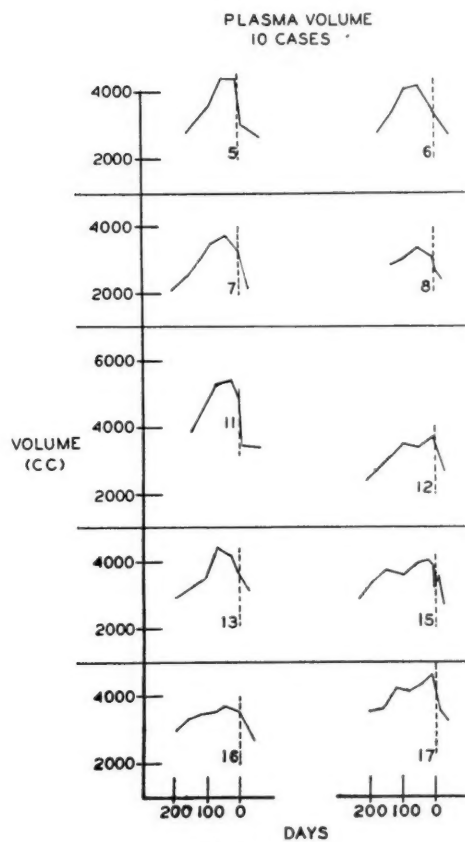
\*Large vessel hematocrit.

Associated with labor and the first thirty hours following delivery, plasma volume continued to decrease. When measured again on the third and sixth postpartum days, an increase in volume was noted. On the thirtieth day after delivery plasma volume had returned to normal limits for body weight.

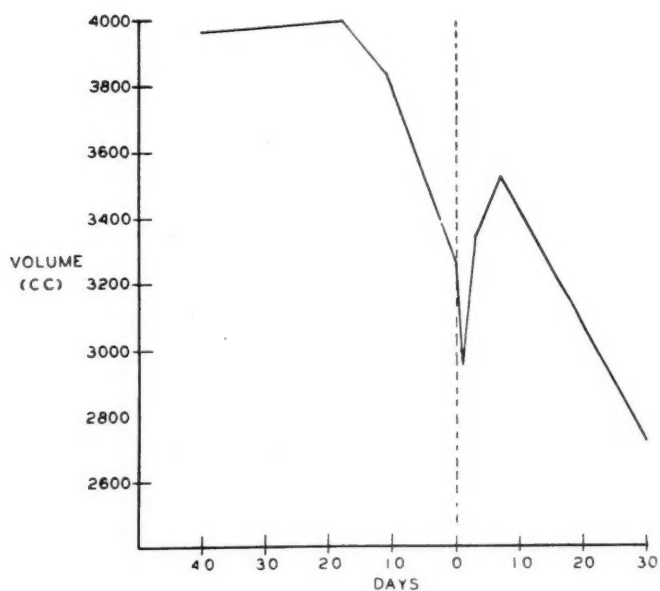
Illustrated graphically in Fig. 3 is the mean per cent plasma volume change of these ten patients. This is based on the mean per cent change from the thirtieth day postpartum volume which has been considered as the non-pregnant normal value for these women. When first observed near the end of the first trimester, the plasma volume was higher than the level subsequently observed thirty days following delivery. A progressive increase in volume then continued until the latter part of the ninth lunar month. The largest individual increase was 72 per cent, the lowest was 36 per cent, with an average increase of 49 per cent over the postpartum nonpregnant levels. There was a 25 per cent prelabor decrease of the total increase of plasma volume which had occurred during pregnancy. No relationship was noted during gestation between weight variations and plasma volume.

*Extravascular Fluid.*—Repeated simultaneous measurements of plasma and extracellular fluid volumes enable one to study the changes which occur both in the vascular and extravascular compartments. These changes in the extravascular fluid volume during pregnancy are illustrated graphically in Fig. 4, in which each individual case is plotted.

In eight of the ten patients studied, extravascular fluid increased throughout the course of pregnancy and there was no prelabor decrease observed. It is apparent from a consideration of Table I that Cases 11 and 13 did not adhere to this pattern. Case 11 had only a total weight gain of 8.5 pounds during pregnancy. In this patient there was no significant difference between the earliest and latest prepartum extravascular fluid-volume observations. During the entire puerperium, this patient had only a 10-pound weight loss with little decrease in extravascular fluid volume. Her weight increase was no doubt due to the growth of the products of conception. This absence of extravascular volume changes is in contrast to that of the other nine patients who gained from 20 to 36 pounds and who during pregnancy had more marked changes



PLASMA VOLUME CHANGES  
ASSOCIATED WITH LABOR  
AND THE PUERPERIUM  
CASE 15



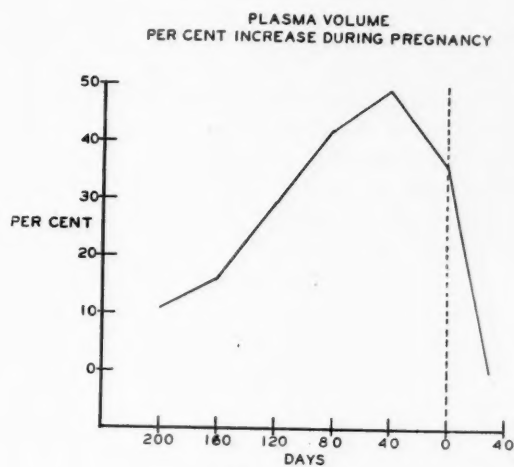


Fig. 3.

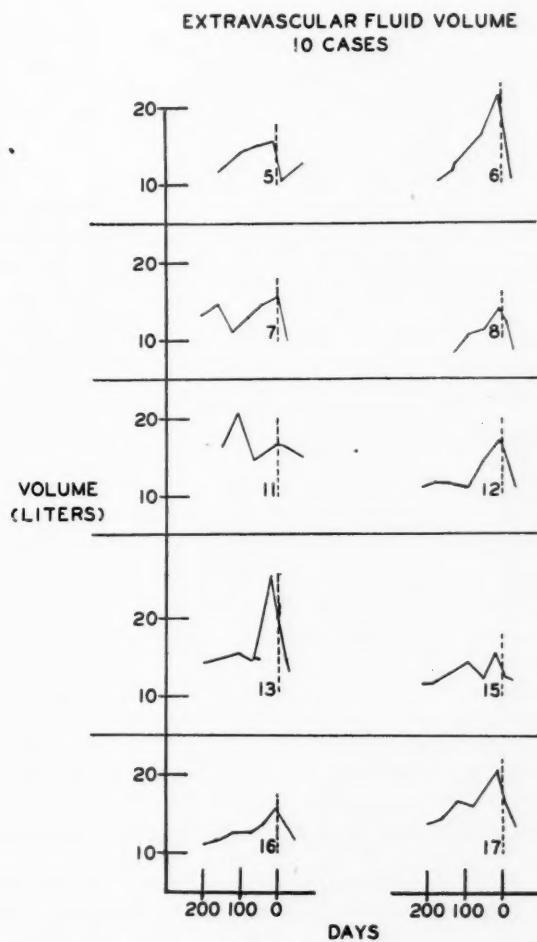


Fig. 4.

in this compartment. This group can be assumed to represent the average pregnant patient whose weight gain is due to both the growth of the conceptus and the storage of water. Case 13 was a patient who had a sudden 13-pound weight gain between the thirty-first and thirty-sixth week of pregnancy. This was associated with an 11 L. increase in extravascular fluid volume. During the next three weeks prior to the onset of labor, there was a 3-pound weight gain with a 5 L. prelabor decrease in extravascular fluid volume. Assuming the determinations to be entirely correct, this suggests a possible shift of fluid from the extravascular to the intracellular space.

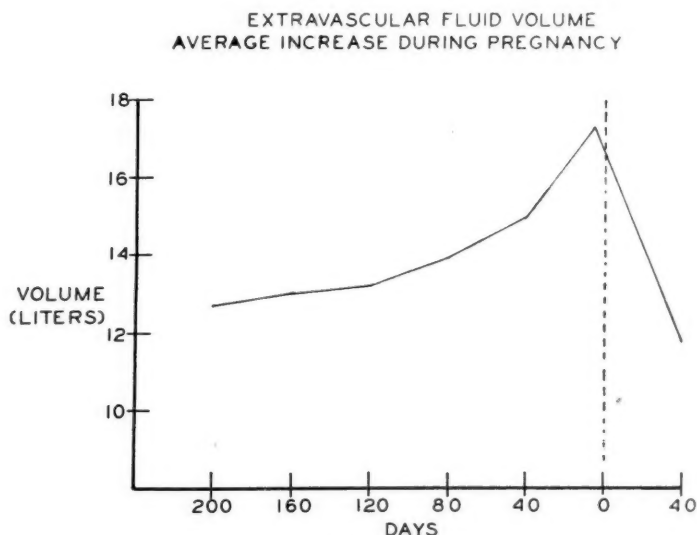


Fig. 5.

In Fig. 5 is illustrated the average extravascular fluid volume for these ten individuals during pregnancy. In the latter part of the first and during the second trimester there was only a slight elevation in the volume of this space, while during the last trimester there was a marked increase. During the period of pregnancy in which the observations were made, there was an average total increase of 4,600 c.c. With the exception of Case 13, the peak volume was reached during the eleven days preceding the onset of labor. In five patients in whom the extravascular fluid volume was measured at the end of the first week in the puerperium, an average decrease of 2,500 c.c. had occurred. The volume of this compartment when measured 26 to 66 days after delivery had decreased 59 per cent from the maximum prepartum increase. These last observations of extravascular fluid volume constituted 19 per cent of body weight which is still greater than the accepted normal nonpregnant value of 15 per cent. This slow decrease in extravascular fluid volume is in contrast to the more rapid return of plasma volume to normal.

#### Selective Retention of Fluid in Plasma and Extravascular Compartments

The vascular and extravascular spaces, which make up the extracellular fluid compartment, retain fluid at different rates and amounts in each trimester of pregnancy. These data are illustrated graphically in Fig. 6, and show the ratio of the absolute changes in extravascular fluid to plasma volume. A significant change in this ratio is first noted approximately 160 days prior to the



onset of labor. Although the volumes of plasma and extravascular fluid are each increasing during the early period of gestation, plasma volume is increasing to a much greater degree than extravascular fluid. This is reflected by a decrease in the ratio between the volumes of the two compartments. The depressed ratio continues through the second and into the first part of the last trimester. Approximately eighty days prior to the onset of labor, there is a marked reversal of the ratio. This change in the ratio is the result of an accelerated increase in extravascular fluid volume which is further augmented by the decrease in plasma volume occurring about the 40th day prior to delivery. At delivery and in the puerperium when checked at seven and thirty days, there is no significant difference in this ratio.

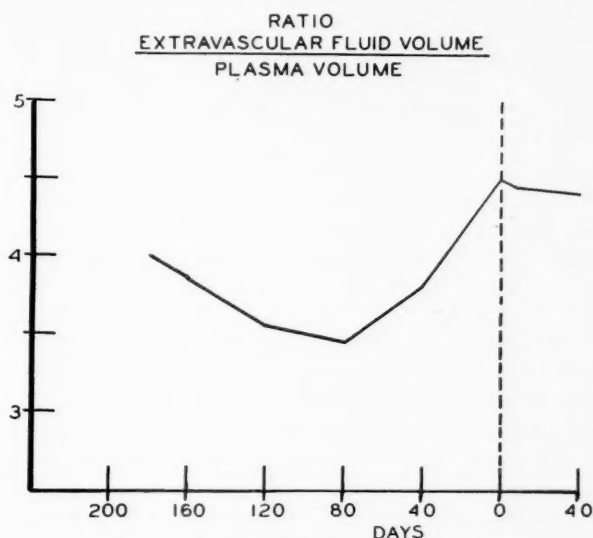


Fig. 6.

### Discussion

These studies are in accord with previous observations that there is a marked increase in plasma volume during the course of pregnancy. Furthermore, there is a prelabor decrease in plasma volume. When the average of the last antepartum plasma volume determination in the patients who went to term is subtracted from the average of the highest antepartum observation, the mean difference is -347 c.c. The standard error of the individual differences is 100.2 c.c.; the ratio of the difference between the two means and the standard error of the differences is 3.73, which proves that the prelabor decrease of plasma volume is statistically significant.

The question arises whether the progressive increase in plasma volume as measured by the dye method is a real increase or whether the results obtained are due to unsuspected sources of error in the method used during pregnancy. Since plasma volumes are based on the disappearance slopes of the injected dye, any factor that would lead to admixture of the dye in fluid compartments in which the dye does not gain access in the nonpregnant state might lead to erroneous results. Two alterations in fluid circulation and balance which are known to occur in pregnancy suggest themselves as possible disturbing factors, namely, an increase in the lymph load and a demonstrated increase in extracellular fluid.

That intravenously injected T-1824 does gain access to the lymph has been established. Ferrebee et al.<sup>8</sup> have measured the amount of dye appearing in the thoracic and cervical lymph of dogs at intervals following injection. In one experiment, 7.5 per cent of the injected dye had appeared in the thoracic lymph in two hours.

Much information can be gained by inspection of the characteristics of the disappearance slopes obtained in the individual plasma-volume determinations. All of the slopes obtained were linear during the sampling period of fifty minutes. In no instance did the dye concentration of individual plasma samples deviate from the general slope of the curve in direction or magnitude sufficient to indicate any recirculation of the dye from the lymphatics into the circulating plasma. Furthermore, the rate of disappearance of the standard quantity of dye injected did not vary by more than 2 per cent in successive determinations in the same individual during the course of pregnancy and the puerperium. The concentration of dye in the initial postinjection sample taken ten minutes later closely approximated the value used in calculating plasma volume. It follows that if an amount of dye sufficient to affect the accuracy of plasma volume determination had entered either the lymph or extracellular fluid compartments, or both, this entry must have occurred during the time in which the dye was becoming mixed in the blood stream, i.e., within the first ten minutes after injection. It would also appear that, if large amounts of dye entered the lymph immediately following the injection, some evidence of the return of lymph-borne dye to the circulating plasma via the thoracic duct would have been found at some time during the sampling period. As stated above, there was nothing in the individual disappearance curves to indicate recirculation of the dye. The results of extravascular fluid volume determinations indicate that there is a continued hydration of this compartment through the last ten days of pregnancy. In the measurements of extravascular fluid volume made in this study, a correction was made according to the method of Crandall and Anderson<sup>9</sup> for the amount of thiocyanate diffusing into the maternal red cells. A more accurate correction figure was obtained by determining the circulating red-cell mass with red cells tagged with radioactive iron, Fe 55.<sup>10</sup> However, it is not possible to determine with this degree of accuracy the thiocyanate diffusion into the amniotic fluid and the fetal and placental mass. The amniotic fluid reaches a maximum volume of 1,000 c.c. to 1,500 c.c. at the seventh month of pregnancy. Following this peak, there is a steady decline and at term the amount is considered to be less than 700 c.c.<sup>11</sup> During this latter phase of gestation there is a progressive increase in fetal mass amounting to approximately 1,600 Gm. The amount of extracellular water in the fetal mass has been determined to lie between 30 per cent and 43 per cent.<sup>6, 12</sup> This would represent a 500 c.c. to 700 c.c. increase in fetal thiocyanate space in the last eight weeks of pregnancy. It will be readily noted that this fetal increase is offset by the progressive decrease in amniotic fluid volume.

The ratio of the changes between extravascular fluid volume and plasma volume suggest a selective or differential retention of fluid in the extravascular compartment. This selective retention rather than a simple hydration first manifests itself about 160 days prior to the onset of labor. From this time and continuing until the 80th day prior to labor, there is a greater percentage increase in plasma volume than in extravascular fluid. Beginning about the 80th day, extravascular fluid volume increases much more rapidly than plasma volume and this process is further augmented by the prelabor decrease in plasma volume.

### Conclusions

1. The plasma volume increased markedly during pregnancy and reached maximum volume during the 68th to 5th day prior to the onset of labor. This increase was 49 per cent when compared with the nonpregnant values thirty days following delivery.

2. There was a statistically significant decrease of plasma volume in the latter weeks of pregnancy, averaging 25 per cent of the total increase which had occurred during pregnancy.

3. Plasma volume had returned to normal nonpregnant values by the thirtieth day after delivery.

4. There was an increase in the amount of extravascular fluid up to the onset of labor. The rate of increase was accelerated during the last trimester with no evidence of any prelabor decrease.

5. In the first week of the puerperium there was a 2,500 c.c. decrease in extravascular fluid volume.

6. The extravascular fluid volume, when measured for the final time between the twenty-sixth and sixty-sixth day of the puerperium, was 59 per cent below the maximum prepartum value.

7. The vascular and extravascular spaces show a retention of fluid which varies in amount in each trimester of pregnancy. During the first and second trimesters, the percentage increase of plasma volume exceeds the percentage increase of extravascular fluid volume. In the last trimester, the percentage increase in extravascular fluid volume is greater than the percentage increase in plasma volume.

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## CERTAIN ASPECTS OF ECLAMPSIA\*

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CONVULSIONS may arise in a woman during her last trimester of gestation from as many different causes as in the nonpregnant female or the male. In addition, the syndrome called eclampsia, characterized by convulsive seizures and other specific signs and symptoms, may occur as a unique complication of late pregnancy.

The etiology of the disease remains unknown, although the number of theories, past and present, proposed to explain its causation is legion. Many of the theories postulated in the past have, at present, only an historical interest. It seems fairly certain now that eclampsia is not due to uremia, bacterial infection, autointoxication, nor to changes in the mammae, nor to edema per se. These theories and others may be discarded because of data which have been accumulated in many hospitals and research institutions.

As a classical example of an outdated theory, the old mammary hypothesis of Sellheim may be cited. This theory was based upon the superficial resemblance between eclampsia and parturient paresis of cattle. We know now that the latter disease in cattle is due entirely to hypoglycemia, and no one today practices mastectomy in the treatment of eclampsia. Unfortunately, the pathogenesis of eclampsia has not been so easy to elucidate.

Even if we do discard many of the older theories which have not been substantiated, we are still left with a rather long list of theories. Since it would be impossible to discuss all these even briefly, we have elected to present a summary of the theories which have been considered in recent years. These have been divided into three main groups, simply for the purpose of classification. There are obviously some injustices in this classification, because certain theories cannot be placed in any particular category; but we hope that the majority of the present-day theories have been included. For a discussion of most of them, we shall be forced to refer you to the several critical reviews of the subject which have appeared in recent years (Browne, 1944, Theobald, 1946, Hofbauer, 1946).

We shall discuss in some detail a few of the theories which hold a particular interest for us. In doing this, we wish to make it clear that we are not attempting to rate any particular theory, based upon adequate data, above or beyond any other theory with an equal amount of data as its background. Furthermore, we are not interested in propounding any particular theory of our own.

\*Address presented before the International Congress of Obstetrics and Gynaecology, Dublin, Eyre, July 8, 1947, by the late Dr. Stander.

†Died May 2, 1948.



First, let us consider those theories which postulate that the fault lies outside the maternal organism. Those which consider the meteorologic influences will be discussed by others here, and may be omitted from this presentation. We can probably dismiss for now, and possibly forever, those theories which postulate some sort of infection as being the instigator of the eclamptic syndrome.

The theory which postulates that the disease is the sequela of a dietary deficiency, either single or multiple, still deserves attention. This theory was originally propounded here in Dublin, although with a somewhat different interpretation from that of today. Nevertheless, it seems appropriate to consider it first. In recent years, this theory has gained new proponents and has been tested in several ways. Clinical experiments have been conducted in which the diet ordinarily consumed during pregnancy has been supplemented with many dietary factors (Ross et al., 1938, Ebbs, Tisdall, and Scott, 1941, People's League of Health Experiment, 1942). The results in general have not been striking. Only in the League Experiment was there a significant decrease in the number of primiparas who developed albuminuria with or without hypertension and/or pre-eclampsia in the supplemented group.

TABLE I. CAUSES POSTULATED OUTSIDE MATERNAL ORGANISM

1. Dietary deficiency
a. General
b. Protein
c. Calcium
d. Vitamin
2. Infection
a. Pyelitis
b. Septic foci to infect placenta
3. Meteorologic influences

Another approach, made by Burke and her collaborators in 1943, has been to conduct a dietary survey during the last trimester of pregnancy. Her data show that 44 per cent of the patients in the "very poor" and "poor" diet groups developed pre-eclampsia and 8 per cent in the "fair" group. There was no pre-eclampsia in the "good" and "excellent" diet groups. These differences are statistically significant; however, when these findings are analyzed on the basis of protein alone, the relationship between low-protein diet and incidence of toxemia is not significant (Stuart, 1947).

It is Theobald's view (1946) that a deficiency in one or more of several factors might lead to the syndrome we call eclampsia. Theobald states, "The dietetic deficiency hypothesis alone satisfies all eclamptic postulates. The evidence in its favor, and in particular that afforded by the geographic distribution of the toxemias of pregnancy, appears very strong. Nevertheless, its proof awaits the satisfactory demonstration that they can be prevented."

Arnell, Goldman, and Bertucci (1945) have also presented evidence to indicate that protein intake may be related to the development of pre-eclampsia and eclampsia. They do not hold the view, however, that protein deficiency is the "only factor in the causation" of the disease. These and other studies (Strauss, 1938, Holmes, 1941, Bibb, 1941, Theobald, 1946), though not conclusive, suggest that diet may definitely play a role in the development of eclampsia and severe pre-eclampsia. Whether its role is primary or secondary remains to be seen.

The classic criticism of the dietary theory has been the observed decrease in the incidence of eclampsia which occurred in parts of Germany during World War I. A similar decrease in the incidence of eclampsia has been reported to have occurred in Holland in World War II during the "hunger winter" of 1945 (Smith, 1947). Any dietary theory of eclampsia, to be valid, must explain these decreases.

We certainly think data should continue to be collected along these lines. Furthermore, efforts should be made to make the dietary data more quantitative. For instance, a diet may be poor in a number of different ways so all data collected on "poor" diets may not be comparable. We could ask, for example, what would have been the incidence of pre-eclampsia in groups, similar to Burke's "very poor" and "poor" groups, receiving supplements sufficient to make each and every one of their diets excellent. We are planning to carry out some experiments in our own clinic which might or might not shed light upon this phase of the problem. We plan to study the nitrogen and mineral balances of patients to determine, first, what the nitrogen balance is in patients with severe pre-eclampsia and, then, whether any dietary factors might affect that balance.

We shall now discuss briefly some of the theories which consider the primary fault to occur in the maternal organism. We shall not consider the constitutional predisposition or the pressure theories, nor those which ascribe the cause to the dysfunction of one particular endocrine gland. We shall outline briefly the development of one theory, proposed as an endocrine hypothesis and subsequently modified. As you all know, Smith and Smith, in 1934, originally observed the blood and urine chorionic gonadotropins to be higher and the estrogens lower in toxemic than in normal patients. These changes, though similar to those which occur, according to the Smiths, in normal cases at the time of labor, start some weeks before the onset of the symptoms of toxemia. There is also a decreased excretion of pregnandiol. The findings were interpreted as indicating a dysfunction in the metabolism of these hormones which led to the toxemic syndrome.

TABLE II. CAUSES POSTULATED WITHIN MATERNAL ORGANISM

1. Constitutional predisposition
2. Pressure theory
3. Endocrine imbalance
a. Pituitary
b. Adrenal cortex
c. Others
4. Chemical poisons
a. Guanidine
b. Histamine
c. Tyramine

Subsequent work, in general, has borne out the observations of the Smiths with regard to the blood levels and the excretion of the hormones. However, the picture has become rather more obscure than clear as more work is done. The data to date along these lines have been summarized by Rubin, Dorfman, and Miller. In general, there is agreement among all workers that the pregnandiol excretion is decreased. Urine estrogens were not always found low, while serum estrogens, where determined, were low in only about 25 per cent of the cases. Urine and chorionic gonadotropins have not been found elevated in all cases. One group of workers reports serum chorionic gonadotropins within normal limits. Such variations certainly suggest discrepancies, the explanation for which must await more data. To speculate, one might wonder how much of this variation may be due to an altered kidney function.

The Smiths have carried their theory further and have more recently observed a toxic euglobulin to occur in the menstrual discharge. They attribute the local vascular changes seen in menstruation to this substance. A substance of similar activity, as judged by the precipitin test, appears in the blood of menstruating and toxemic women and in pleural exudates. This toxin also seems to have marked fibrinolytic activity associated with it, which may be a separate factor. This enzyme is also present in the euglobulin fraction of the blood, and they postulate that tissue damage from any cause releases a proteolytic enzyme (the fibrinolysin?) which in turn yields a labile toxic protein.

Late toxemias of pregnancy, therefore, might be due to a withdrawal of hormonal support resulting in the elaboration of the toxin. The reasons for the withdrawal of the hormonal support seems, in their theory, to be due to an inadequate supply of blood to the placenta. The primary cause of eclampsia, then, becomes any mechanism or factor which interferes with the blood supply of the uterus. The changes from normal which they have observed in the hormonal pattern and the toxin thus apparently become sequelae to the decrease in blood supply. But why does the blood supply decrease?

The hormonal theory, particularly as it relates to the female sex hormones, is attractive and intriguing because there is such a marked change in the concentration of these hormones during pregnancy. However, rather than speculate, let us await more evidence on the normal metabolism of these substances.

Next, we shall consider briefly the histidine hypothesis as an example of the theories which postulate an amine as being responsible for the eclamptic syndrome. As you know, this theory was postulated in 1926 by Hofbauer. It now has a new exponent in Kapeller-Adler, who observed a histidinuria in normal pregnancy (1934). This observation seems to have been amply confirmed. More recently she has observed a histaminuria to accompany the histidinuria in several complications of pregnancy (1941). Subsequently, she reported (1943) a histaminuria accompanying the histidinuria in seven out of ten cases of hyperemesis gravidarum, in three out of ten cases of threatened abortion, and in twelve out of sixteen cases of mild pre-eclampsia. Only traces of histidine and of histamine were found in the urine in ten cases of severe pre-eclampsia and eclampsia. On the basis of these and other data, she postulates that "histidine and histamine play a significant part in normal and toxemic pregnancy." Further, "The fact that histamine has been isolated from the urine of patients suffering from pre-eclamptic toxemias, as well as from urine of women suffering from hyperemesis gravidarum, suggests that pre-eclamptic and eclamptic toxemia, toxemic vomiting, and premature separation of the placenta may not represent independent diseases, but may form only different manifestations of the same disease, probably an intoxication by histamine." The histamine arises, it is assumed, by the dysfunction of histidine decarboxylase and histaminase. These enzymes can be affected by a number of factors, but whether they are or not is another question.

The finding of histidine and histamine in the urine during pregnancy is of interest, but one doubts whether the sweeping generalizations are at all justified from the data in hand. Furthermore, if severe pre-eclampsia and eclampsia are due to histamine, we should expect some amelioration of the symptoms by the antihistamines. If these drugs do lessen the severity of the disease, the histamine theory certainly will be greatly enhanced. But we are still faced with the question of how and where is the histamine produced in excess? We can also ask why the histidinuria of pregnancy? Is it due to an increase in the amount of histidine metabolized or due to an inability of the kidney to reabsorb histidine? Page's data (1946) indicate that the latter might be the case. But if so, why? It is known, for instance, that histidine is not required for the maintenance of nitrogen balance in the adult male (Rose et al., 1943). But is it required by the pregnant female? Does the fetus require it for growth? We can go on asking such specific questions, the answers to which may be obtained by direct experiment in many cases, and when we have enough of these answers we may be able to evaluate more competently the histidinuria and histaminuria of pregnancy and the complications of pregnancy.

Finally, we shall discuss a few aspects of the various theories involving the placenta as the site of the genesis of the eclamptic syndrome. It seems, in the end, that many of the theories do come to involve the placenta, and then there is

usually something outside the placenta, which is postulated to bring about the change in the placenta. Such a state of affairs shows that we are really ignorant of the actual cause of the disease or the sequence of changes which occur during its development. Theoretically, one can make an excellent case for the placenta's being involved in the development of the disease, and actually this has been done by many writers. You all know of Young's infarct theory and how it has grown to require an X factor which in turn, due possibly to a vitamin deficiency, leads to disturbance of the endocrine metabolism, probably by interfering with the maternal circulation in the placenta (Young, 1942). This in turn leads to the placental infarction, the products of this necrosis eventuating in eclampsia.

Bartholomew (1936) explains the development of the placental infarcts in a different way. The hypercholesterolemia of pregnancy plus a diet rich in cholesterol leads to an excessive storage of cholesterol in the arteries of the placental villi. This storage enhances or predisposes this area to potential infarcts, the actual precipitating factor being fetal movements. Page (1939), as a working hypothesis, considers the placenta to behave as the kidney and that any condition which tends toward uterine ischemia might cause the liberation of a pressor substance from the placenta, much as the kidney liberates a pressor substance after its circulation has been constricted by a Goldblatt clamp. The theory propounded by the Smiths also seems now to go back to the placenta, requiring an alteration in the uterine circulation for the subsequent liberation of a toxin and/or alteration of the hormonal balance. Dexter and Weiss (1941), too, are of the opinion that, "The present evidence points to the placenta as the 'intra-uterine factor' responsible for toxemia of pregnancy. But probably the renal humoral factor of the pre-existing hypertension has a deleterious effect on the placental circulation, enhancing the development of the characteristic degenerative process in the placenta." Dieckmann (1941) likewise considers the placenta as being indirectly responsible for the liver lesions seen in eclampsia. The constant entrance of chorionic tissue fibrinogen from the placenta into the circulation consumes the proteolytic enzymes which normally destroy proteins absorbed from the intestines. The proteins in the portal circulation then cause the liver damage.

TABLE III. CAUSES POSTULATED WITHIN PRODUCTS OF CONCEPTION

A. Placenta
1. Infarct
2. Ischemia
3. Crush syndrome
4. Allergy
5. Elements
B. Fetus
1. Endocrine imbalance
Adrenal cortex
2. Iso-immunization
a. Rh factor
b. Other factors

We are not going to attempt to evaluate these theories. Nor is it worth while trying to determine which one is correct. We are quite willing to concede that the placenta may well be involved in the development of the disease. But the stage at which it becomes involved is still undetermined.

Finally, as far as theories go, we can probably rule out isoimmunization as an etiological factor, since Hurst, Taylor, and Wiener (1946) found no significant difference in the incompatible blood groups in infants or mothers with toxemia from those in mothers without toxemia, and no correlation between toxemia and Rh incompatibility.



It seems, then, that there are enough theories. We now need more data, and especially data to explain the small, consistently observed phenomena which occur during eclampsia. Until these can be explained, there is no particular point in trying to determine the over-all picture. We do not mean to imply that such work is not being done in the field, for it is, but more is needed.

Let us cite, as an example of what we mean, the work has been going on in our own laboratories. We have no particular theory of eclampsia, so we are quite willing to go whither the data will take us. We were inclined to believe, at one time, that the hyperuricemia of pregnancy was due to liver damage. But we were able to show, by studying the clearance of uric acid and urea, that the hyperuricemia and the hyperuremia in the majority of cases are due, at least in part, to an altered kidney function. That nitrogen retention does occur can be seen by comparing the blood chemistry values in normal pregnancy (in early labor) with the blood chemistry values obtained on admission upon the cases of antepartum and intrapartum eclampsia. These and other data will be shown in a brief presentation of the more important statistics on 76 eclamptic patients admitted to our hospital during the past fourteen years and will serve to illustrate certain of the more outstanding laboratory findings.

In order that one may interpret properly certain marked changes noted in eclampsia, the average, as well as the lower and upper limits, of the blood chemical values found in normal pregnancy are presented in Table IV. It will be noted that the nonprotein nitrogen and urea nitrogen tend to lower values at term, returning toward normal nonpregnant figures on the third postpartum day. The blood uric acid seems unaffected by normal gestation, while the carbon dioxide combining power reveals the well-substantiated compensated "acidosis" of pregnancy as labor is approached. On the third postpartum day, the alkali reserve, as shown by the carbon dioxide values, is nearing the normal level.

TABLE IV. BLOOD CHEMISTRY VALUES IN NORMAL PREGNANCY

BLOOD CONSTITUENT	EARLY LABOR		THREE DAYS POST PARTUM	
	NUMBER OF CASES	VALUE	NUMBER OF CASES	VALUE
Nonprotein nitrogen	13	23 Limits 20-26	10	28 Limits 24-36
Uric acid	13	3.1 Limits 1.7-4.4	10	3.0 Limits 1.9-5.4
CO <sub>2</sub> combining power	13	46 Limits 40-51	9	55 Limits 49-60
Urea nitrogen	13	9.0 Limits 6.1-12.0	10	11.7 Limits 8.1-18.6

TABLE V. TIME OF ADMISSION BLOOD CHEMISTRY IN ANTEPARTUM AND INTRAPARTUM ECLAMPSIA

TIME DAYS	ANTEPARTUM		ANTECONVULSION	
	NUMBER OF CASES	PER CENT	NUMBER OF CASES	PER CENT
5 or more	15	39.5	9	23.7
4	1	2.6	0	-
3	2	5.3	1	2.6
2	9	23.7	4	10.5
1	3	7.9	8	21.0
0	7	18.4	14	36.9
1	1	2.6	2	5.3
Total	38		38	

As most chemical and metabolic studies on eclampsia have been made only during the height of the disease, we have attempted to obtain blood and urinary determinations prior to the outbreak of the eclampsia. From Table V it will be seen that blood studies were performed five or more days prior to the first convulsion in 23.7 per cent and prior to delivery in 39.5 per cent of the patients. In slightly over one-third of the patients, the first chemical study was made at the time of the convulsion or shortly thereafter.

TABLE VI. AVERAGE BLOOD CHEMISTRY VALUES IN ANTEPARTUM AND INTRAPARTUM ECLAMPSIA, 46 CASES

CONSTITUENT	ON ADMISSION	AT HEIGHT OF DISEASE*	ON DISCHARGE
N. P. N. mg. per cent	32	39	33
Uric acid mg. per cent	4.4	6.6	3.3
Urea N. mg. per cent	12.1	15.9	11.5
CO <sub>2</sub> vol. per cent	42	43	53
Chlorides mg. per cent (as NaCl)	500	493	489

\*As judged by elevation in nonprotein nitrogen and uric acid.

These blood chemical values, as well as those at the height of the disease, are averaged in Table VI. The striking findings are increased nonprotein and urea nitrogen and uric acid. All the values are essentially normal at the time of discharge. Although the carbon dioxide values on admission are close to normal, markedly low figures are seen following the development of convulsions, as shown in the last column of Table VII.

TABLE VII. CARBON DIOXIDE COMBINING POWER IN ECLAMPSIA

TIME OF SPECIMEN	NUMBER OF ANALYSES	AVERAGE CO <sub>2</sub>	RANGE OF CO <sub>2</sub>
Admission	38	42	26-55
24 hrs. AC	18	43	27-54
12 hrs. AC	4	45	37-49
8 hrs. AC	4	33	23-42
4 hrs. AC	-	-	-
2 hrs. AC	2	40	37-43
1 hr. AC	1	49	-
Less than 1 hr. PC	26	33	23-47
1 hr. PC	6	38	28-48
2 hrs. PC	5	45	40-53
4 hrs. PC	5	43	38-47
12 hrs. PC	17	44	34-58
24 hrs. PC	27	45	32-58
Discharge	45	53	46-66

AC—Anteconvulsions

PC—Postconvulsions

The patients who received sodium lactate because of a low CO<sub>2</sub> combining power are not included in this table.

TABLE VIII. UREA CLEARANCE IN EARLY PUERPERIUM FOLLOWING ECLAMPSIA

DAYS FOLLOWING DELIVERY	ANTE- AND INTRAPARTUM		POSTPARTUM	
	NO. CASES	UREA CLEARANCE % OF NORMAL	NO. CASES	UREA CLEARANCE % OF NORMAL
5-8	17	98	4	110
9-12	17	91	9	104
13-16	6	93	4	79
17-24	2	99	2	74
No record	9	--	6	--
Average		94		96
Average of all				95

In each of the 61 of the 76 antepartum, intrapartum, and postpartum eclamptic patients in whom the urea clearance was determined, the kidney function, as shown by this test, was within normal limits at the time of discharge (Table VIII).

The type of delivery is shown in the following table (Table IX). Twenty-six per cent of the ante- and intrapartum and sixty per cent of the postpartum eclamptic patients had a spontaneous vaginal delivery. Almost half the former group and only 6.7 per cent of the latter had forceps delivery. We were greatly surprised to see the very high incidence of breech delivery, 12 per cent and 19 per cent in the ante- and intrapartum, and postpartum, groups, respectively. Cesarean section was performed in a relatively small number of these patients, 14 and 3.8 per cent, respectively, in the two groups. It is also interesting to note that four of the 26 patients with postpartum eclampsia had twins.

TABLE IX. TYPE OF DELIVERY IN ECLAMPSIA, 76 CASES

TYPE OF DELIVERY	ANTE- AND INTRAPARTUM		POSTPARTUM	
	NUMBER OF CASES	PER CENT	NUMBER OF CASES	PER CENT
Spontaneous	13	26.0	18	69.2
Operative:				
Forceps	24	48.0	2	7.7
Breech	6	12.0	5	19.3
Section	7	14.0	1	3.8
Total	50	100.0	26*	100.0

\*Four of these 26 patients had twin pregnancies and in each case the second twin presented by breech.

In the 68 patients with vaginal delivery, labor was induced in 38.3 per cent (Table X).

TABLE X. TYPE OF INDUCTION IN ECLAMPTIC PATIENTS WITH VAGINAL DELIVERIES, 68 CASES

TYPE OF INDUCTION	NUMBER OF CASES	PER CENT
Medical	11 <sup>1</sup>	16.2
Rupture of membranes	8 <sup>2</sup>	11.8
Bag	5	7.4
Bougie	2	2.9
Total	26	38.3

<sup>1</sup>Includes one postpartum case.

<sup>2</sup>Includes three postpartum cases.

The maternal and fetal mortalities are shown in Table XI. The uncorrected maternal mortality was 1.3 per cent and the gross fetal 29 per cent. The latter group is further analyzed in Table XII, which shows the great majority to have been macerated or deadborn.

TABLE XI. MATERNAL AND FETAL MORTALITY IN ECLAMPSIA, 76 CASES

TYPE OF DELIVERY	MATERNAL MORTALITY		FETAL MORTALITY	
	NUMBER OF CASES	PER CENT	NUMBER OF CASES	PER CENT
Spontaneous	—	—	12	15.8
Operative	1*	1.3	10	13.2
Total	1	1.3	22	29.0

\*Low forceps.

TABLE XII. FETAL MORTALITY IN ECLAMPSIA, 22 CASES

TYPE	DELIVERY		TOTAL	PER CENT
	SPONTANEOUS	OPERATIVE		
Macerated	7	2	9	40.9
Deadborn	3	3	6	27.3
Stillborn	1	—	1	4.5
Died*	1	5	6	27.3
Total	12	10	22	100.0

\*Within four days of delivery.

Finally, a follow-up study is depicted in Tables XIII and XIV. From these, it would appear that 66 per cent of the patients for whom we have follow-up records have no hypertension six weeks after the cessation of the disease, and only about 15 per cent show a persistent hypertension. Of the 76 eclamptic patients, 19 had subsequent pregnancies, although this is undoubtedly far too low a figure, as most of these patients were not seen after their six-weeks postpartum examination following the eclampsia. However, of the 19 known to us to have had a subsequent pregnancy, two had severe pre-eclampsia and three mild pre-eclampsia in these subsequent pregnancies.

TABLE XIII. SUBSEQUENT COURSE FOLLOWING ECLAMPSIA, 76 TOTAL CASES

SIX WEEKS BLOOD PRESSURE	NUMBER OF CASES	PER CENT
Below 140/90	38	51.3
Above 140/90	20	26.3
No record	18	22.4
Total	76	100.0

20 CASES WITH BLOOD PRESSURE ABOVE 140/90 AT SIX WEEKS POST PARTUM

BLOOD PRESSURE	NUMBER OF CASES	PER CENT
Below 140/90 later	9	45
Stays above 140/90	9	45
No record	2	10

TABLE XIV. SUBSEQUENT OBSTETRIC HISTORY OF ECLAMPTIC PATIENTS, 76 TOTAL CASES

SUBSEQUENT PREGNANCY	NUMBER OF CASES	PER CENT
No record of subsequent pregnancies	57	75.0
One subsequent pregnancy	15	19.7
Two subsequent pregnancies	4	5.3
Total	76	100.0

23 CASES WITH SUBSEQUENT PREGNANCY

COMPLICATION	SUBSEQUENT PREGNANCIES	
	ONE	TWO
No complications	6	3
Severe pre-eclampsia	2	—
Mild pre-eclampsia	2	1
Abortion	1	1
Ectopic	0	1
Deadborn	—	2
No record of outcome	4	—
Total	15	8

The laboratory findings presented above have not taken us very close to the core of the problem; however, we have learned a little about eclampsia and more about the utilization of the blood chemical findings in the treatment of the



disease. Furthermore, as a by-product, we have learned something about kidney function, because the clearance studies revealed a competition between diodrast and uric acid, which has been of value in studying kidney tubular function. By continuing these studies, we hope we shall be able to follow a path which will lead us nearer to the solution of the problem.

There are many such paths which need studying. Some of them are and have been receiving attention; others not, possibly because our knowledge of physiology is still limited in this particular field.

In conclusion, may we say that the etiology of eclampsia, although unknown at present, should be discoverable by the application of the scientific method. A theory of eclampsia should be, then, a working hypothesis to be tested by experiment.

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## THE TREATMENT OF ADVANCED CARCINOMA OF THE OVARY\*

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IN A previous paper, one of us (E. V. H.)<sup>1</sup> reported a survey of one hundred cases of cancer of the ovary treated by eighteen surgeons on the gynecologic services of the Elizabeth Steel Magee and the St. Francis Hospitals, Pittsburgh, Pennsylvania. Thirty-seven of these cases were on the service of the senior author.

The cases were classified clinically as follows:

*Group I.*—The tumor is completely removable and is apparently confined entirely to the ovary.

*Group II.*—The tumor is completely removable but with adhesions or involvement of other structures that can be removed.

*Group III.*—The tumor is only partly removable on account of extension to other structures.

*Group IV.*—The tumor is irremovable because of extensive involvement of adjacent parts, and only a biopsy is feasible at operation.

In seventy-six of the cases an attempt was made to remove the primary growth and variable amounts of the metastatic growth. In a follow-up study of a hundred patients, sixty-five of them were traced from admission to the hospital to ten and two-thirds years after operation. Thirteen cases are alive from one and one-fourth years to ten and two-thirds years after operation, but to date only four survived five years or more.

With results such as these the question may be asked, why operate on these patients? It is the purpose of this paper to answer this question from our experience with operation alone or operation followed by x-ray therapy.

We believe that operation is indicated:

1. To definitely establish the diagnosis and extent of the disease. (Tuberculous peritonitis, endometrial nodules in the cul-de-sac, nodular chocolate cysts of the ovary, or benign tumors with ascites may simulate ovarian cancer.)

2. In Groups I and II, because there is a probability that all of the malignant growth can be removed.

3. In Group III the cancer is no longer confined to the ovary, but has spread to the viscera and parietal peritoneum and often the omentum, and is frequently associated with ascites. One of the chief purposes of this paper is to discuss the treatment of this group. The condition is 100 per cent fatal if allowed to run its course without operation. X-ray therapy alone has not been curative. When the disease has advanced to the stage where the diagnosis of clinical Group III

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can be made, the patient is doomed to a most uncomfortable, semi-invalid or invalid existence for her remaining days. Any salvage of life in this group is very unusual but it may occur and constitutes a surgical triumph.

For a long time there has been an impression that removal of the primary ovarian growths in the presence of metastatic nodules on the peritoneum may prolong the life of the patient, and in a few cases may result in disappearance of the outlying implants. We are not too much interested in the prolongation of life in patients with malignant disease unless it is accompanied by a reasonable degree of comfort to the patient and a life of usefulness.

In the following group of cases, the first case may indicate that life has been saved. In the remainder, the patients have been entirely or at least reasonably comfortable and they have been able to carry on a life of usefulness for a limited time in contrast to the life of invalidism which confronted them when they first appeared for examination. They came to us because of pain and/or enlargement of the abdomen.

### Case Reports

CASE 1.—S. R. K., single, aged 49 years, St. Francis Hospital Gynecological No. 35-263, was admitted June 19, 1935. *Diagnosis.*—Papillary adenocarcinoma of the left ovary with metastases to the peritoneum, left broad ligament, and sigmoid colon. *Chief Complaints.*—Pain on defecation (two months), watery stools (two to three years), and abdominal enlargement of one week's duration. She had a normal menstrual history, except three months of amenorrhea recently followed by a menstrual period for three days and then spotting for three weeks. The abdomen was enlarged, and an irregular lobulated mass was felt reaching to the umbilicus. There was evidence of free fluid in the peritoneal cavity. A barium enema revealed no intrinsic lesion in the colon.

*Operation.*—June 22, 1935. Cauterization of the cervix, supravaginal hysterectomy, bilateral salpingo-oophorectomy. There was a large quantity of bloody fluid in the abdomen. There was a large papillary cystadenocarcinoma of the left ovary which was partly intraligamentous. The sigmoid colon was adherent over it. Masses of carcinoma had broken through the capsule into the broad ligament and were scooped out with the hand, leaving carcinomatous tissue on the sigmoid and in the broad ligament. The right ovary seemed normal. No lesions of the colon or stomach were found. Three gauze drains covered with a sheet of gutta percha were placed over the operative field and brought out through the lower end of the incision. Six hundred fifty cubic centimeters of whole blood were given during the operation. *Diagnosis.*—Papillary cystadenoma malignum of the ovary. Following the operation x-ray therapy was given over the lower abdomen. On Oct. 2, 1935, the patient felt well and was gaining in weight, a small mass was felt in the left side of the cul-de-sac. On Feb. 8, 1936, the patient looked well and had gained 20 pounds in weight. When seen in 1945 she had been teaching school since one year after operation and felt well. There was no evidence of extension of the growth over this span of ten years.

CASE 2.—Mrs. M. Z., aged 48 years, St. Francis Hospital Gynecological No. 33-279, was admitted on July 31, 1933. *Diagnosis.*—Cervical polyp, intraligamentous papillary cystadenoma malignum of ovaries with metastases. *Symptoms.*—Bleeding from rectum for ten days, loss of weight in the last six months, fullness of abdomen, and mass felt in abdomen. Patient ceased menstruating six months ago but with occasional spotting since then. She has had one child and two miscarriages. There was a firm mass in the pelvis extending to above the level of the umbilicus in the left side. There was evidence of free fluid in the abdomen. A small polyp protruded from the cervix. The above mass felt cystic, and small nodular masses were present in the cul-de-sac. There were signs of fluid in the left chest, and the chest was tapped and 900 c.c. of clear yellowish fluid were removed (Meig's syndrome). The next day this was repeated and 1,350 c.c. of fluid were removed.

*Operation.*—August 8, 1933. Removal of cervical polyp, cauterization of the cervix, laparotomy and removal of a large quantity of fluid from abdomen. A cystic intraligamentous left ovary about 15 cm. in diameter and a similar cyst on the right side about 8 cm. in diameter were removed. There were nodules on the peritoneum and intestines, and much of the omentum was involved. A large portion of the omentum was excised. Six gauze drains and a sheet of gutta percha were placed over the raw surfaces in the pelvis. Six hundred cubic centimeters of whole blood were given during the operation. *Diagnosis.*—Papilocystadenoma malignum of ovaries, and secondary papillary cystadenoma malignum of peritoneum and omentum. Patient made a good recovery and was seen last in June, 1937, four years after operation. She had been carrying on her vocation as a midwife until that time. She stated then that her abdomen seemed larger and that she was losing weight. On examination no evidence of fluid or tumor was made out and a note was made that the patient "looks as though she should have recurrence of growth, but no evidence is felt except an adherent uterus, and the abdomen seems to be in remarkably good condition considering what was found and what was left at time of operation." In the follow-up in 1945 we learned that she is dead, but we could not learn how long she lived after our last examination, four years after operation. *NOTE.*—Patient had no recurrence of fluid in abdomen or chest and was able to carry on her work as a midwife for at least four years.

*CASE 3.*—Mrs. M. K., aged 50 years, St. Francis Hospital No. 46,571, was admitted April 12, 1942. *Diagnosis.*—Papilocystadenocarcinoma of the right ovary with generalized abdominal carcinomatosis. *Symptoms.*—Abdominal enlargement and pain. She had had multiple operations in the past on the kidneys, gall-bladder, and had had appendectomy and bilateral salpingectomy. The abdomen had been tapped on several occasions before her present admission to the Hospital. On examination a firm, irregular mass filled the lower abdomen to the level of the umbilicus, and there was marked ascites present. A cystic feeling, fixed mass was present in the cul-de-sac. *Operation.*—April 16, 1942. Approximately 4,000 c.c. of slightly blood tinged fluid was evacuated from the peritoneal cavity. On exposing the mass, a large gray-white, fungating, friable surface was found. The mass was adherent to the pelvic structures and particularly to the uterus and small intestines. Peritoneal implants were present over much of the abdomen. The mass was separated and removed with difficulty. It seemed to arise from the right ovary. Five gauze drains and a sheet of gutta percha were placed over the operative field. Five hundred fifty c.c. of whole blood were given during the operation. *Pathologic Diagnosis.*—Papillopseudomucinous cystadenocarcinoma of the ovary. X-ray therapy was started three weeks after operation. On June 30, 1942, the patient was getting along satisfactorily. A movable nodule was felt in the cul-de-sac, but no masses or fluid were detected in the abdomen. On July 22, 1943, the patient was getting along fairly well. She complained of inability to gain strength, but she looked better. The mass in the cul-de-sac seemed somewhat larger, but there was no evidence of fluid in the abdomen. In answer to the follow-up letter in January, 1945, she wrote that she had some abdominal pain but was able to be up and about and do housework, and tapping had not been necessary since before operation. On April 18, 1945, she was seen at the Tumor Clinic and the following note made: "The patient has only one complaint and that is of intestinal cramps when her bowels move or after taking a laxative. She has gained weight and feels quite well generally. No palpable masses in the abdomen. Considerable thickening of the skin and many hemangiectases of the skin over the lower abdomen which is a postradiation effect." *NOTE.*—Patient has been able to carry on her home duties for three years with no recurrence of ascites, although she had been tapped several times before operation.

*CASE 4.*—Mrs. J. S., aged 42 years, St. Francis Medical No. 88,008, was admitted Jan. 29, 1944. *Diagnosis.*—Papillary cystadenocarcinoma of both ovaries, ascites. *Complaints.*—Feeling of heaviness and enlargement of the abdomen of one month's duration, and flatulence. Patient menstruated regularly and normally. No history of pregnancies. On examination



the abdomen was enlarged and there was a distinct fluid wave present. The right ovary was cystic and about 5 cm. in diameter, and the left ovary was about 12 cm. in diameter.

*Operation.*—February 8, 1944. Papillary growths were found on the external surface of the right ovary. No papillary growths were seen on the left ovary, but on opening it after operation the internal wall of the cyst was covered with papillomatous growths, and some areas of the walls seemed solid. The omentum was studded with papillary growths, and there was a large quantity of reddish-brown fluid in the peritoneal cavity. Total hysterectomy, bilateral salpingo-oophorectomy, and resection of the omentum were done, and gauze drains were placed in the pelvis and carried out through the vagina. On March 1, 1945, the patient felt well and had been carrying on her usual activities. No evidence of fluid or nodules was made out on abdominal and pelvic examination. *NOTE.*—This patient has been restored to normal for thirteen months and there is no evidence of recurrence.

*CASE 5.*—Miss A. H., aged 42 years, Elizabeth Steel Magee Hospital, No. 32129, was admitted on July 8, 1937. *Diagnosis.*—Papillary cystadenocarcinoma of both ovaries. *Complaints.*—A sense of weight and pressure in the bladder for six months. A mass in the abdomen had been noticed for three weeks. Menstrual periods occurred every three weeks in the last two years, and they lasted from seven to ten days. There was a smooth, rounded, slightly tender, somewhat movable tumor felt in the lower abdomen extending for three fingerbreadths above the umbilicus. On vaginal examination with one finger, several nodules were felt beneath the tumor, and the base of the tumor felt fixed. *Operation.*—July 9, 1937. Both ovaries were replaced by masses of papillomatous, friable growth that extended on to the uterus and pelvic peritoneum and fixed the genitals to the surrounding structures. The omentum contained many papillomatous masses. The removal of the pelvic organs was difficult due to obliteration of the landmarks. Bilateral salpingo-oophorectomy, supravaginal hysterectomy, and resection of the omentum was done. Five gauze drains were placed so as to cover the remaining oozing carcinomatous operative field. They were covered with a piece of gutta percha and the drains were brought out of the lower end of the incision. Ovarian masses measured approximately 7 by 10 cm. each and contained very little tissue that could be identified as ovary. *Diagnosis.*—Papillary cystadenocarcinoma of both ovaries with extension to the uterine wall and omentum. Patient made a good recovery and returned to her vocation as schoolteacher in September, 1937. On vaginal examination small residual masses were felt in each adnexal region. On Dec. 27, 1938, one and one-half years after operation, the patient returned complaining of cramps in the left lower quadrant, and flatulence of three days' duration. There was vomiting, and the patient stated that the bowel movements had been getting smaller. A freely movable mass, about 3 cm. in diameter, was felt in the left lower quadrant, presumably in the sigmoid colon, and barium enema revealed a constriction in the sigmoid colon. The signs of partial intestinal obstruction subsided, and the patient was given a course of x-ray therapy. The mass in the left lower quadrant became smaller until it was barely palpable and the patient felt well. The masses in the cul-de-sac remained the same. She resumed teaching in September, 1939. Because of some jaggings pains at times in the right lower quadrant, another course of x-ray therapy was given in the Fall of 1939 and again in the Spring of 1940, when the pelvic masses seemed larger. She resumed her teaching following this treatment. On Aug. 12, 1940, she was admitted to the Hospital because of partial intestinal obstruction, and on Aug. 23, 1940, a colostomy was performed. She went home on Sept. 22, 1940, and died on Aug. 14, 1941. *NOTE.*—Except for one episode of partial intestinal obstruction for a few days, the patient was comfortable for three years. She had three courses of x-ray therapy because of residual masses in the pelvis, but was able to carry on as a schoolteacher. Three years after her original operation a colostomy was necessary because of intestinal obstruction. She lived another year but not in comfort or as a useful citizen.

*CASE 6.*—Miss A. G., aged 21 years, Elizabeth Steel Magee Hospital, No. 64933, was admitted on Aug. 21, 1944. *Diagnosis.*—Papillary cystadenocarcinoma of both ovaries. *Complaints.*—Pain in right side off and on for three years, and lump in the right side noticed recently. Menstrual history normal. A nodular, tender mass was visible and palpable in the right

lower quadrant. On vaginal examination the uterus was found small and pushed forward, and there was a mass in the right side and behind the uterus that was firm, nodular, and fixed, and about 15 cm. in diameter. At operation on Aug. 23, 1944, both ovaries were found much enlarged and nodular. Large fungating, granular masses extended through the capsules of both ovaries and involved the surrounding structures. Small nodules were scattered over the uterus, bladder peritoneum, cul-de-sac, sigmoid colon, appendix, and a few in the omentum. No involvement of the upper abdomen was made out. Hysterectomy and bilateral oophorectomy were carried out. Three gauze drains covered by a gutta percha drain were placed over the raw surfaces in the pelvis. *Pathologic diagnosis.*—Papillary cystadenocarcinoma of ovaries. Deep x-ray therapy was started before the patient left the hospital, and was continued later with the patient ambulant. She had arranged to be married on Oct. 1, 1944, and this plan was discouraged, although she was not told about her true condition. Her fiancé in the Armed Forces was told about her condition, and he insisted on going through with their plans in order that he might turn over his allotment to her when he was overseas, and they were married. On Feb. 5, 1945, the patient felt quite well, had gained in weight; a nodule was palpable in the cul-de-sac. On May 5, 1945, the patient looked well and felt well, she continued to gain in weight and accepted a clerical position and was working daily. The nodule in the cul-de-sac seemed unchanged.

CASE 7.—Mrs. E. P., aged 31 years, Elizabeth Steel Magee Hospital, No. 455, was admitted on Oct. 12, 1935. *Diagnosis.*—Papillary cystadenocarcinoma of the ovary with extension to the peritoneum, omentum, and intestines. *Symptoms.*—Tenderness and pain in the lower abdomen. A mass in the abdomen had been noticed for three weeks. Normal menstrual history except that some clots were passed in the last three months. One child 7 years old. Patient has felt tired recently, and three weeks ago noticed a mass in the lower abdomen. A hard, nodular mass was present in the lower abdomen, reaching for three fingerbreadths' above the pubis. At operation on Oct. 14, 1935, about 500 c.c. of straw-colored fluid, containing flakes of fibrin, was found in the peritoneal cavity. Numerous nodules were present in the omentum. The pelvic organs were matted together in a solid, cancerous growth involving both ovaries, the peritoneum, and intestines. Nodules were felt under the diaphragm. The uterus, both ovaries, and the omentum were removed. Five gauze drains and a sheet of gutta percha were placed over the raw surfaces in the pelvis. *Pathologic diagnosis.*—Adenocarcinoma of both ovaries with extension to the uterine surface and omentum.

The patient had postoperative x-ray therapy. On March 5, 1936, a note was made that the patient looked well and felt well, she drove her own car and had been skiing with her husband. She expected to leave for Florida in three weeks. On examination a nodule 2 cm. in diameter was felt on the right side of the cul-de-sac.

July 23, 1936.—The patient felt well and had gained in weight, pelvic examination as before.

April 7, 1937.—The patient felt well and had returned from her second trip to Florida where she spent three months. She was to take another course of x-ray treatments.

Nov. 17, 1937.—The patient felt well. She was eating and sleeping well, and her weight was increasing. The nodule in the cul-de-sac remained the same.

March 7, 1938.—Patient returned with a history of passing some blood in the urine. She has lost weight recently. On examination there was induration on both sides of the cul-de-sac and evidence of fluid in the abdomen. The patient died on April 4, 1938. NOTE.—This patient lived in comfort and carried on her usual activities for more than two years after operation.

CASE 8.—Mrs. C. S., aged 45 years, Elizabeth Steel Magee Hospital, No. 35,427, was admitted on April 24, 1938. *Diagnosis.*—Papillary cystadenocarcinoma of the left ovary with extension to the peritoneum and intestines. *Complaints.*—Pain in the left lower quadrant and left leg—severe, of one week's duration; loss of weight for three months; and nausea and

vomiting for one month. She menstruated regularly, was pale, and had a sallow color. Hemoglobin was 62 per cent. The uterus was displaced to the right by a mass in the left adnexal region about 8 cm. in diameter. It was not very tender, but the mobility was limited. Impression—malignant growth of the left ovary. Patient had an operation in another city in 1936, and it was learned that at that time she had an adherent papillomatous cyst of the right ovary, and that the appendix and right ovary had been removed and the diagnosis of cyst of the right ovary with intracystic papillomas, nonmalignant, had been made. At operation on May 4, 1938, we found a large papillomatous cyst of the left ovary adherent to the sigmoid and small intestine. In the region where the right ovary had been removed there was a mass of carcinomatous tissue about 4 cm. in diameter. As much of this tissue as seemed feasible was removed, along with the uterus and left ovary. There was no evidence of tumor in the upper abdomen. Gauze drains were placed against the oozing surfaces where malignant tissue had been removed, and they were covered with gutta percha. Blood transfusion was given during the operation. *Pathologic diagnosis.*—Papillary cystadenocarcinoma of the ovary. X-ray therapy was started while the patient was in the hospital, and it was continued later with the patient ambulant. She was completely relieved of the pain in the left lower quadrant and down the left leg.

In November, 1940, the patient was still feeling well and had gained thirty pounds in weight. Three months later she developed edema of the abdominal wall and the legs, and she died two months later. NOTE.—This patient had complete relief from pain for two and one-half years after operation and x-ray treatment, and was able to carry on her usual activities.

CASE 9.—Mrs. G. G., aged 43 years, Elizabeth Steel Magee Hospital, No. 60238, was admitted on Aug. 17, 1943. *Diagnosis.*—Papillary cystadenocarcinoma of the ovaries with extension to the peritoneum and broad ligaments. She complained of pain and enlargement in the lower abdomen for the past two months, and frequent menstruation (every two weeks). She had a normal menstrual history until two months ago. She had no children, but had had one miscarriage. There was a tense, cystic, moderately tender mass visible and palpable in the lower abdomen, and it extended up to the umbilicus. The uterus was pushed forward by the mass. No nodules were felt, but the tumor was adherent. At operation on Aug. 18, 1943, a large, cystic left ovary was filled with a brown fluid. The left ovary and right adnexa were adherent and the adhesions of the left ovary to the colon were indurated with tumor tissue. There were nodules scattered over the peritoneum of the uterus and anterior cul-de-sac and in the broad ligaments. A total hysterectomy and bilateral salpingo-oophorectomy were done. The oozing surfaces in the pelvis were covered with gauze drains which were carried down into the vagina. *Pathologic diagnosis.*—Papillary cystadenocarcinoma of the ovary (mesonephroma type). On Sept. 3, 1943, x-ray therapy was started.

June 12, 1945.—The patient was symptom free and vaginal examinations were negative for nodules. Three weeks before the patient began to have pain in the left lower quadrant and shortly afterward she noticed swelling of the left leg. On examination there was tenderness and induration in the region of the left brim of the pelvis and along the left pelvic wall. The vault of the vagina was healed and pliable, and no other masses were felt. Another course of x-ray therapy was given. NOTE.—This patient has been free of symptoms and has been able to carry on her usual activities for practically two years, she is now under treatment again with x-ray.

CASE 10.—Mrs. G. P., aged 43 years, St. Francis Hospital Gynecological No. 35-186, was admitted on April 26, 1935. *Diagnosis.*—Secondary adenocarcinoma of the ovary; adenocarcinoma of the hepatic flexure of the colon. *Symptoms.*—Cramps in lower abdomen and diarrhea for eight weeks, and loss of weight. She had a normal menstrual history, except for slight bleeding every two days for the last month. She had had two children. She had lost 15 pounds of weight in the last two months.

The patient was a thin emaciated woman who looked anemic and who weighed 96 pounds. Red blood cells, 3,310,000, and hemoglobin 60 per cent. There was a firm, fixed mass in the pelvis reaching to the umbilicus, and which pushed the uterus forward. No nodules were felt, but the mass was fixed. *Operation*.—May 1, 1935. Cauterization of the cervix, bilateral salpingo-oophorectomy. The omentum was adherent over a pelvic mass, and about 100 c.c. of serosanguineous fluid was found in the peritoneal cavity. A large, irregular mass about 20 cm. in diameter replaced the right ovary, and a loop of ileum was adherent to it. The mass was ruptured, and friable tissue escaped in separating the adhesions. The left ovary seemed negative. Four gauze drains and one sheet of gutta percha were placed over the operative site. At the hepatic flexure of the colon was a hard, irregular movable mass about 7 cm. in diameter and involved the whole circumference of the colon. No enlarged glands were felt, and no nodules were detected in the liver. The patient was given 1,200 c.c. of whole blood during the operation. *Pathologic report*.—Adenocarcinoma of the ovary and Fallopian tube. At a second operation on May 22, 1935, the terminal ileum, cecum, ascending colon, hepatic flexure, and one-third of the transverse colon were resected, and ileo-colostomy done. A blood transfusion of 1,200 c.c. was given during operation. *Pathologic report*.—Adenocarcinoma of the colon. The patient made a satisfactory recovery from both operations and was discharged on June 12, 1935, with a red blood count of 3,850,000, and hemoglobin of 86 per cent. On Oct. 14, 1935, patient had gained in weight and had been doing her own housework, but there was a cystic mass in the cul-de-sac which was aspirated and bloody fluid obtained. X-ray therapy was given, and the bowels were loose.

January 9, 1936.—Diarrhea continued, and the patient had lost weight. She died on March 8, 1936, thirteen months after operation.

In the above ten cases, the average survival time has been three years and one month. (This survey was completed in June, 1945.) In January, 1948, thirty-one months later, Cases 1, 3, 4, and 6 are known to be still alive and comfortable.

The following two cases are suggestive, but do not necessarily indicate that the poor results were obtained because operation was not followed by radiation therapy.

CASE 11.—Mrs. S. M., a 42-year-old, thin, white woman was admitted to the Elizabeth Steel Magee Hospital on April 2, 1944, with a chief complaint of lower abdominal pain and backache. The pain dated from 1942, at which time she gave birth to a stillborn anencephalic monster. This had been her only pregnancy. Before the present admission she had nausea and vomiting for two months. A mass was found in the left lower quadrant. A diagnosis of left ovarian cyst with adhesions was made. At operation the cyst was adherent to the sigmoid, and a supravaginal hysterectomy and bilateral salpingo-oophorectomy were done. *Pathologic diagnosis*.—Papillary cystadenocarcinoma of ovary. She was advised to return for x-ray therapy, but failed to do so. She returned to the Hospital with malignant invasion of the bladder and rectum, and died on March 14, 1945, less than twelve months after operation.

CASE 12.—Mrs. M. M., a 56-year-old, well-nourished white woman, the mother of ten children, was admitted to the Elizabeth Steel Magee Hospital on July 17, 1943, complaining of a tender mass in the left lower quadrant. The menopause had occurred fourteen years before, and there had been no vaginal bleeding since then. For three months prior to admission there was difficulty in getting her bowels to move. There was no loss of weight. A left ovarian cyst was found, and operation advised. On opening the abdomen a cyst about 15 cm. in diameter was found adherent to the parietal peritoneum. None of the other pelvic structures was grossly involved. Malignancy was not expected from the gross appearance, and simple removal of the cyst was performed. *Pathologic diagnosis*.—Multilocular papillary cystadenocarcinoma of the ovary. The patient was advised to return for x-ray therapy but refused. She died on April 4, 1945, less than nine months after operation.



A third case illustrates the futility of radiation therapy in advanced cases where it is not feasible to remove the tumor.

CASE 13.—Mrs. N. F., a 54-year-old, robust, white woman was admitted to the Elizabeth Steel Magee Hospital on April 30, 1945, with a chief complaint of lower abdominal pain, associated with frequency of urination and difficulty in defecating. Cystoscopic examination revealed invasion of the bladder wall, and proctoscopic examination revealed marked narrowing of the lumen of the colon. On pelvic examination there was a fixed irregular mass filling the entire left side of the pelvis. Operation was not advised, and radiation therapy was started. This was soon discontinued on account of the marked reaction. The patient became worse rapidly and died on May 27, 1945, twenty-seven days after admission. In addition to this case, two others were studied in which radiation therapy alone was given, the cases being too far advanced to undergo operation. Both failed to improve and were dead within two months of admission.

### Discussion

Nine of the above twelve cases which were operated upon were from 42 to 50 years of age. One patient was 56 years old. The other two were 21 and 31 years of age, respectively (Cases 6 and 7), and they lived the normal life of a young woman for a limited time. In Case 6 the patient is still alive and apparently well in 1948.

In some of these cases, removal of the primary growths at first seemed surgically impossible without causing the death of the patient. With careful evaluation of how much operative work the patient could stand and with care in determining the proper lines of cleavage, it was possible to remove the primary tumors, and often masses of outlying growth were scooped out with the hand, leaving behind irremovable malignant tissue. Usually hemorrhage is not severe when working through this type of tissue, and with the aid of blood transfusions during the operation, the primary operative mortality in our own personal series has been low. It is our practice at the end of such operations to cover the operative field in the pelvis with gauze drains over which is placed a sheet of gutta percha. This quickly controls oozing, and the field is walled off by adhesions early and prevents unimpeded extension of the disease through the peritoneal cavity. The gauze drains are removed under light anesthesia in one week.

When there is ascites present, and at times tapping is required frequently, if there is much involvement of the omentum, resection of the involved omentum may eliminate the ascites or greatly prolong the intervals between tapping. In Cases 2, 3, 4, and 5, there was no recurrence of the ascites. In Groups I and II, total hysterectomy and removal of both adnexa should be done whether the disease is unilateral or bilateral. In Group III, the tumor is not completely removable, and this procedure is modified according to conditions, and supravaginal instead of total hysterectomy is usually done. As stated before, the Group III patients have tolerated these extensive operative procedures quite well, the primary mortality has been low, and we are willing to accept a low primary mortality in order to accomplish the results reported. In the Group IV cases, exploratory laparotomy and biopsy alone cannot be done with impunity, as deaths have occurred following this procedure. A careful evaluation of the patient's condition must be made in all cases in order to determine the feasibility and extent of the operative procedure.

The frequency of secondary carcinoma in the ovary has led us to explore the gastrointestinal tract for a primary growth, in all cases of carcinoma of the ovary. The results in carcinoma of the ovary, when it is secondary to carcinoma of the gastrointestinal tract, have been poor as to cure or length of life, because the ovarian carcinoma is already a metastasis from a primary growth. It is in the papillo-cystadenocarcinoma group that operation followed by x-ray therapy seems to increase the duration of life and the comfort of the patient.

In some cases, after operation, when the residual tumor grew and caused pain again, decrease in the size of the tumor and relief of pain followed repetition of x-ray therapy (Cases 5 and 9). Because of these observations, it is felt that x-ray therapy probably prolongs the life of the patient to some extent.

We share the pessimism of most operators in regard to the final results in Group III cases, but do not agree with the practice of some in opening and closing the abdomen without attempting the removal of the primary growth when the disease has spread beyond the ovary.

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## CUTANEOUS VASCULAR CHANGES IN WOMEN IN REFERENCE TO THE MENSTRUAL CYCLE AND OVARECTOMY

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THIS report deals with vascular changes in the skin of women in relation to the activity of the ovaries. Two groups of observations are included. The first concerns cyclic variations in cutaneous pigments and blood flow in normal women. The second consists of similar observations in women after ovariectomy. The spontaneous, momentary flushing of the castrate state was not studied. The investigation concerns, rather, more permanent changes in the skin. The effects of estrogen and progesterin upon skin following ovariectomy, were also tested.

Recording spectrophotometry of the intact skin was employed. This technique provides an objective and accurate method of observation which can be utilized over many areas of the body and possesses certain advantage over previous methods. This technique has been used in a similar study of castrated men.<sup>9</sup>

The prototype of cutaneous reaction to ovarian secretion is to be found in the reactions of the "sexual skin" of monkeys. This zone includes the vulva, perineum, buttocks, and contiguous areas. The "sexual skin" is not apparent in males or immature females, but begins to be red and turgid in pubescent females, and maintains this character, with cyclic increase, throughout maturity.<sup>1, 7</sup> Its relation to ovarian functions is further shown by its regression after ovariectomy. The dermis in this area consists of loose meshed mucoid connective tissue. The vessels are relatively large and numerous and, though the hairs are sparse in this region, the arrector pili muscles are exceptionally developed and show greater reactivity than elsewhere.<sup>3, 16</sup> The cock's comb is a similar cutaneous area which reacts to gonadal hormones.<sup>13</sup>

Cyclic activity of the sexual skin of monkeys is manifest by redness, swelling, and erection and bristling of the hairs. The swelling is due to an increase in the water content of the mucoid connective tissue, suggesting the premenstrual edema of some women. Activity begins after menstruation, and reaches its height during the third week of the cycle, to subside some time before the onset of the next menstruation.<sup>1, 3, 7, 15</sup>

The peak of activity has been correlated with ovulation and the discharge of estrogenic hormone by the ovary. The output of estrogen shows two peaks—one in the middle of the cycle and the other just before menstruation. After ovulation the follicle begins to produce progesterin, which reaches its maximum in the last few days of the cycle.<sup>2</sup>

The influence of estrogen has been shown experimentally by its ability to induce sexual skin activity in ovariectomized and immature female monkeys,

as well as in males.<sup>1</sup> Progestin has also been shown to induce some hyperemia of the area. However, it is noteworthy that, given simultaneously, progestin inhibits the effects of estrogen on the sexual skin.<sup>14</sup> Once estrogen has stimulated the area, the response is diminished noticeably by the fifth or sixth day after the administration of progestin. If the two hormones are continued, involution of the sexual skin is induced by the fifteenth or twentieth day, which may resemble that of the ovariectomized animal. Under some experimental conditions, progestin appears to *modify* rather than simply to *antagonize* the action of estrogen.<sup>2</sup>

Skin reactivity in monkeys is not absolutely limited to the area of the sexual skin. Bachman et al.,<sup>4</sup> by giving extraordinary doses of estrogen, have caused a reaction beyond the usual confines of the sexual skin, as well as a redness of the face. Likewise, Hisaw, Greep, and Fevold<sup>14</sup> have induced a redness of the face as well as of the sexual skin by giving progestin to an ovariectomized monkey. Mortimer et al.<sup>17</sup> have observed a hyperemia of certain areas of the nasal mucosa concomitant with the activity of the sexual skin. With reference to premenstrual retention of water in the body, Krohn and Zuckerman<sup>15</sup> have demonstrated that swelling of the sexual skin accounts for only a fraction of the total edema, the additional water being distributed in the remainder of the skin as well as in other tissues.

Direct observations have been made of the vessels of living animals after giving estrogen or progestin. Reynolds et al.<sup>18</sup> found that estrogen dilates the small vessels of the ear of ovariectomized rabbits. Mortimer and his co-workers<sup>17</sup> have observed that giving estrogen causes engorgement of vessels in the nasal mucous membrane of monkeys of both sexes.

Few observations in the human being have been reported and they have been quite limited as regards the areas of skin examined. The effects of estrogen and progestin on the circulation in the finger have been studied by several workers. Carloni<sup>6</sup> observed the looped capillaries of the nail fold of normal women. He found that both estrogen and progestin produced vasodilatation, with an increase in the background coloration of the fold and a diminution in capillary pressure. The effect of estrogen was noted in one-half hour and it lasted for the four hours' duration of the experiment. The dilatation induced by progestin was intense within two hours but was shorter in its duration. Carloni further found a difference in the site of action of the two hormones. Estrogen, although it caused an enlargement of the entire vascular loop, acted particularly on the arterial limb, so that its size almost equaled that of the venous segment. Progestin, on the other hand, gave preponderantly a dilatation of the venous half of the capillary loop. Reynolds and his associates<sup>19</sup> studied the effect of estrogen on the nail fold capillaries in women in the menopause. They found a dilatation of the postarteriolar capillaries and venules associated with a diminution in blood flow.

The influence of the menstrual cycle on the state of the nail fold capillaries was also studied by Carloni. He found evidence of vasoconstriction in the early part of the cycle, with vasodilatation in the latter half. His results are somewhat at variance with those of Hagen.<sup>12</sup> Hagen's results, showing vasospasm in the two days preceding menstruation and vasodilatation during menstruation, are open to the criticism that they are based mainly on one cycle in one individual.

Brewer<sup>5</sup> tested the fragility of the cutaneous capillaries in the antecubital and infraclavicular fossae of women. He found an increased fragility which appeared abruptly on the first day of the cycle and lasted for two or three days. He attributed the fragility to vasospasm.



### Material and Methods

Cyclic changes in the skin were studied in five normal young white women. It was assumed that the cycles were ovulatory inasmuch as they were regular, and the menses of moderate duration.<sup>20</sup> Further normalcy of the subjects was indicated by the circumstance that each had been pregnant at least once. Only two of the five subjects were studied for more than one cycle. The pertinent data relating to these two subjects are as follows:

SUBJECT	AGE	PREVIOUS PREGNANCIES	DURATION OF CYCLE	CYCLES STUDIED
R. B.	35	1	28 days	3+
M. W.	28	2	32 days	3

Readings were made five to seven days apart.

In addition to the five normal subjects, three ovariectomized white women were studied.\* Spectrophotometric readings of the selected areas of skin were made before the administration of the hormones. Estrogen and progestin were administered to the ovariectomized subjects, and readings were taken subsequently at intervals of several weeks. Treatment was then discontinued so that the skin might return to its pretreatment state. Estrogen and progestin were used singly and in combination. A summary of the pertinent data is given in Table I.

TABLE I. SUMMARY OF DOSAGE IN OVARIECTOMIZED SUBJECTS

SUBJECT	AGE	TIME AFTER OPERATION	ESTROGEN	TIME OFF TREATMENT	PROGESTIN	COMBINED HORMONES
M. H.	36	2 months	Progynon-B 1 mg. 3 times weekly for 12 weeks	8 weeks	Proluton 5 mg. 3 times weekly for 5 weeks	Proluton 10 mg. } Progynon-B 1 mg. } Once weekly for 3 weeks
E. M.	38	9 months	Progynon-B 1 mg. 3 times weekly for 12 weeks	9 weeks	Proluton 10 mg. 2 times weekly for 5 weeks	Proluton 10 mg. } Progynon-B 1 mg. } 2 times weekly for 2 weeks
E. P.	33	One ovary: 5 years. 2nd ovary: 7 months	Progynon-B 1 mg. 3 times weekly for 4 weeks Di-ovocyclin 1 mg. 2 times weekly for 4 weeks	8 weeks	Proluton 5 mg. 3 times weekly for 5 weeks	Proluton 5 mg. } Di-ovocyclin 1 mg. } 3 times weekly for 2 weeks

*Progynon-B*: Alpha-estradiol-benzoate, in oil. Schering.

*Di-ovocyclin*: Alpha-estradiol-dipropionate, in oil. Ciba.

*Proluton*: Progesterone, in oil. Schering.

All administration was intramuscular.

In both normal and ovariectomized groups, readings were taken of areas of the skin of the trunk, as well as on the upper and lower limbs. The face, hands, and feet were found to be unsuitable, since they are subject to change through exposure to sunlight and other influences, including unusual lability of the circulation. Because of these factors, we were unable to obtain basal conditions in these latter areas. This was unfortunate since there is evidence that face, hands, and feet may be influenced by sex hormones. At any rate, we can say with certainty that if changes did occur in the hands and feet they were not of the magnitude we had observed in the case of male castrates.

\*Referred from the Free Hospital for Women, through the courtesy of Dr. John Rock.

The spectrophotometric determinations were made in a room in which the temperature was maintained at about 70 to 72° F. The relative humidity was kept between 10 and 30 per cent. "The subjects rested for from twenty to forty minutes before readings were begun. Areas of the body habitually uncovered by clothes, such as the hands, were measured last, to allow additional time for the circulation to reach stability. As far as possible, we avoided taking readings at night or soon after meals, since a peripheral vasodilatation may be present at these times.

"A description of the Hardy recording spectrophotometer and a discussion of its use in measurement of the cutaneous pigments have been presented elsewhere.<sup>8</sup> Briefly, the apparatus records the reflectance of the intact living skin, giving an analysis by wave lengths over the entire visible spectrum, from the violet end at 400  $m\mu$  to the red end at 700  $m\mu$ . In the curve thus obtained, each pigment is identified by its characteristic absorption band. The amount of the pigment is indicated by the degree of absorption at the wave length of the band. Lowering of the reflectance at the particular wave length is therefore proportional to the amount of the pigment present. Previous analysis of normal individuals had demonstrated five cutaneous pigments: namely, melanin, a derived material described as melanoid, carotene, reduced hemoglobin and oxyhemoglobin."<sup>9</sup>

Melanin gives marked absorption in the violet end of the curve, since its band lies in the near ultraviolet. Melanoid shows an absorption band at 400  $m\mu$ . The bands of carotene are located at 455 and 482  $m\mu$ . Ordinarily the band at 455  $m\mu$  is obscured by the absorption of hemoglobin, and only that at 482  $m\mu$  is evident.

The spectral characteristics of oxyhemoglobin and reduced hemoglobin deserve special attention, since these two materials are the ones found to be involved in the skin changes of our subjects. Their absorption bands and the change in the curve with differing concentration are shown in Fig. 1.

### Observations

*Normal Cyclic Changes.*—In normal women fluctuations were found in the two forms of hemoglobin but not in the other skin pigment. In the first week of the cycle, the skin curves showed a small quantity of hemoglobin, with a preponderance of the reduced form. These characteristics of the curve became slightly more pronounced by the time of the mid-cycle (Fig. 2). In our experience, such skin curves represent a sluggish cutaneous blood flow, but without any associated venous dilatation. From mid-cycle on, there was a steady increase in both the quantity of hemoglobin and the proportion of oxyhemoglobin, reaching a maximum in the day or two preceding the onset of menstruation. We construe these changes as indicating a great increase in blood flow in the skin. The change from an active flow at the end of the cycle to a sluggish flow in the beginning of the cycle occurred at about the time of onset of menstruation. More frequent readings than we have made would be necessary to localize the time more exactly.

It is noteworthy that these cyclic variations in blood flow were observed over the entire trunk and at least the upper parts of the limbs. There is suggestive evidence that the face, and the hands and feet, may share in these changes. Yet, for the reasons mentioned earlier, we felt obliged to exclude these zones from our final analysis.

*Postovariectomy Changes and Effects of Administration of Estrogen and Progestin.*—Subjects M. H. and E. M. showed essentially the same findings

through their respective courses of observation. Subject E. P., who had had one ovary removed five years, and the second seven months, before the study, showed inconsistent results, suggesting the presence of a remnant of ovarian tissue, or of some extragenital source of material supplanting the ovarian hormones.

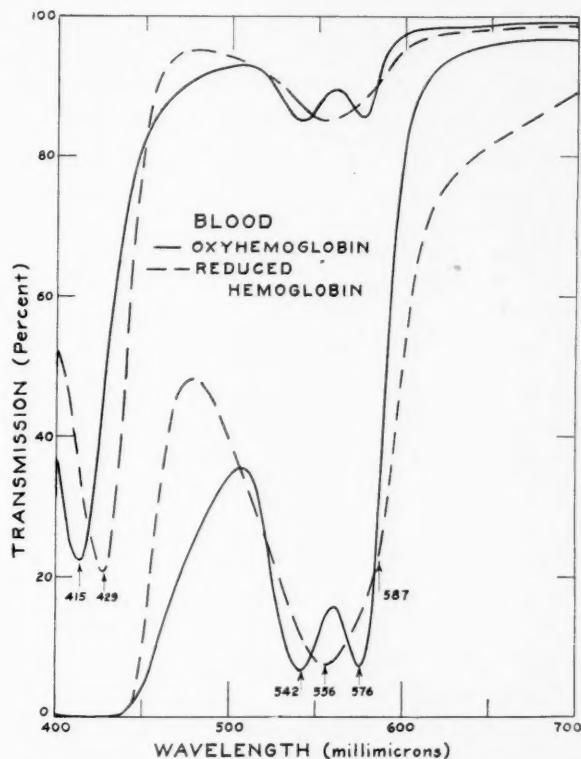


Fig. 1.—The transmission of reduced and oxyhemoglobin. In the lower curve the blood was diluted 1 to 100; in the upper curve it was diluted 1 to 1,600. Oxyhemoglobin shows a pair of absorption bands at 542 and 576  $m\mu$ . In reduced hemoglobin these bands are replaced by a single band at 556  $m\mu$ . The general shape of the curves is also useful in determining the relative quantities of these two materials.

Ovariectomy did not remove those pigmentary characteristics which distinguish the female from the male. As previously reported,<sup>8</sup> these are as follows: The female skin shows less melanin and less hemoglobin than the male. Areas primarily rich in melanin show a comparatively higher melanin ratio over poorly pigmented areas than is the case in the male. The buttocks are predominantly arterial (high in oxyhemoglobin) in the female, while they are predominantly venous (high in reduced hemoglobin) in the male. There is more carotene in the female breast, abdomen, and buttocks than in the corresponding regions in the male.

Only one variation from the normal occurred in the female castrate—a diminution in the total amount of hemoglobin, with a slightly increased proportion of reduced hemoglobin over oxyhemoglobin. These findings probably represent a diminution in the cutaneous blood flow.

We had found similar changes in male castrates, but it was apparent that the change in females was somewhat less marked in degree. Moreover, there was no clear evidence of venous dilatation in the more "venous" areas of the body, such as had been observed in the male subjects.

The effect of the administration of estrogen was to increase the amount of hemoglobin present and to accentuate the twin absorption bands of oxyhemoglobin (Fig. 3). We interpret these findings to indicate an increase in cutaneous blood flow. A single large dose given to subject, M. H., when she was off treatment elicited the effect within four hours.

When the subjects were taken off estrogen, the curves reverted to their pre-treatment levels. However, upon the administration of progestin, oxyhemoglobin increased again. The effect of progestin was somewhat more marked than that of estrogen in heightening the ratio of oxyhemoglobin to reduced hemoglobin. The total amount of hemoglobin varied and was often diminished by the treatment. It should be noted that neither hormone gave as much increase in blood flow as had been seen in male castrates after testosterone.

The combined use of estrogen and progestin was not long tolerated by the subjects, mainly because of the advent of pain in the breasts. After combined administration, the curves showed a striking lack of hemoglobin and an increase in the proportion of the reduced form. We interpret this as evidence of a sluggish blood flow.

### Discussion

Our observations show that ovariectomy does not entirely change the basic peculiarities which distinguish the female from the male skin. Similarly, the male castrates previously studied had maintained to some extent, their differences from the female. In both sexes, therefore, we can assert that sex differences are basically due to genic influence. This base line of pigmentary characteristics is then modified by the presence of the sex hormones. Unlike the situation in many other animals, where reactivity to the hormones is localized in special areas, the human skin reacts probably in its entirety.

In the male castrates, where the greatest changes were in hemoglobin as related to cutaneous blood flow, there were, in addition, some variations in the other skin pigments as well. A striking reduction was found in the total amount of hemoglobin with a relative increase in the proportion of the reduced form. In areas with a large venous bed, a real increase in reduced hemoglobin was observed, suggesting venous dilatation. A slight diminution in melanin formation occurred with an increase in the derived pigment melanoid. Finally, carotene storage increased in the entire integument. All of these changes could be reversed by the administration of testosterone propionate. In females, ovariectomy induced a reduction and sluggishness of blood flow but the more static pigments were not affected. Moreover, no evidence of venous dilatation was noted in areas with normally extensive venous networks, such as was seen in the men.

The part played by estrogen and progestin in the correction of the ovariectomized state has been demonstrated. Each given singly increased the cutaneous blood flow. Estrogen gave a volume increase as well, which progestin did only inconsistently. Our findings are in general agreement with the evidence of former workers that these materials produce vasodilatation. It is known that the entire blood volume of the ovariectomized patient is diminished but will increase again on the giving of estrogen.<sup>11</sup> That this alone could be responsible for the increase in cutaneous blood volume seems unlikely in view of the rapidity with which the administration of estrogen alters the skin curve.



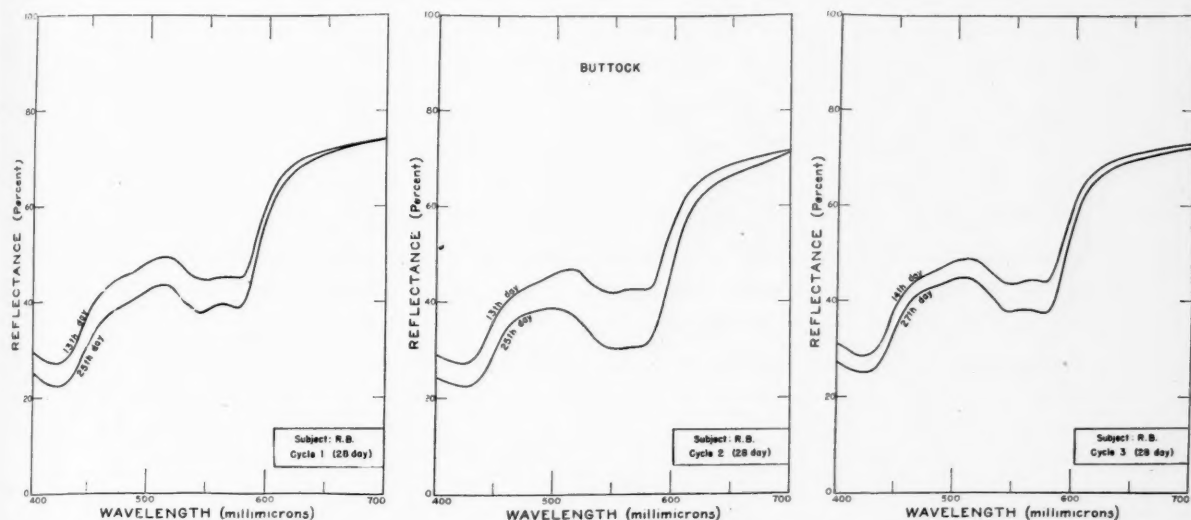


Fig. 2.—Normal cyclic change in the spectrophotometric curves of the buttocks during three successive cycles. In each cycle the earlier curve shows little hemoglobin, which is rather poorly oxidized. The later curve shows an increase in hemoglobin, with dominance of the oxidized form.

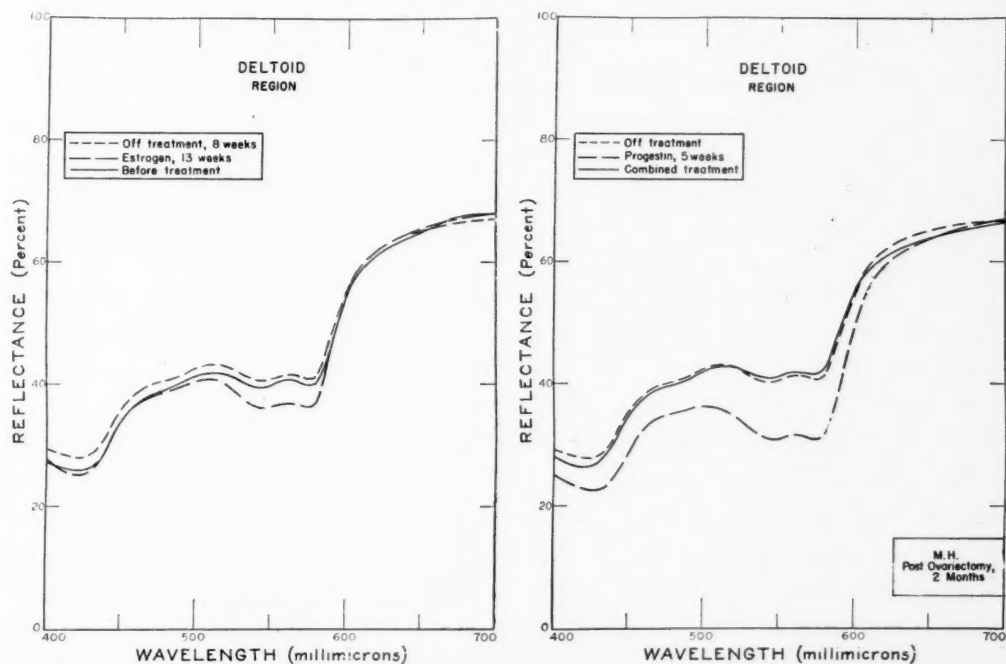


Fig. 3.—Spectrophotometric curves of the deltoid region of an ovariectomized subject. On the left, the pretreatment curve is low in hemoglobin content, and with dominance of the reduced form. After treatment with estrogen, the curve shows a real increase in oxyhemoglobin. With cessation of treatment, the curve reverts to its pretreatment character.

On the right the administration of progesterin produces a marked increase in oxyhemoglobin. The combined use of progesterin and estrogen diminishes the hemoglobin content causing the curve again to revert to its off-treatment level.

There is sufficient tide in the levels of estrogen and progestin in the intact woman to account for the appearance of the skin in the first half of the cycle. At this time there is neither much estrogen nor progestin in the body (Fig. 4). As the follicle ripens, estrogen is formed but does not reach high levels until late in the cycle. It is at this time that the skin curve indicates a more active blood flow. The two additional features of the activated sex skin of the monkey, edema and pilomotor activity, may also be represented in the human being. Premenstrual edema of women is a well-recognized entity, but, to our knowledge, increased pilomotor activity has not been reported. However, personal clinical observation enables us to assert that increased pilomotor response can be demonstrated in women at about mid-cycle.

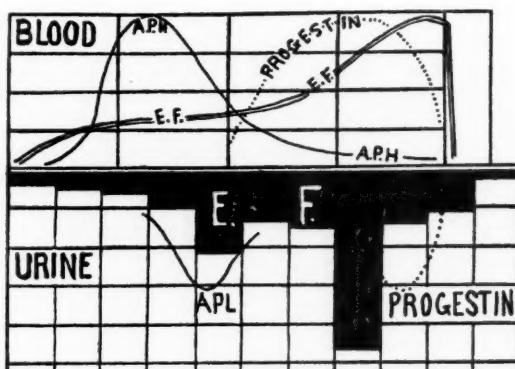


Fig. 4.—Current concepts of the cyclic tide of the female sex hormones, from Frank.<sup>10</sup> E. F., estrogenic factor. A. P. H., anterior pituitary gonadotropic hormone. A. P. L., anterior pituitary-like gonadotropic hormone.

The progestin curve of the blood is theoretical, by deduction from measurements of pregnandiol excretion in the urine.

Progestin becomes appreciable in the latter half of the cycle. We have seen that the simultaneous administration of the two hormones diminishes the amount of cutaneous blood and its activity so that it resembles that of the castrate state. It would seem paradoxical that the curves of normal women continue to show an increasingly active flow in the latter few days of the normal cycle. This paradox is resolved if we recall the observation of previous workers that the modification by progestin, of estrogen influence on the sex skin of monkeys, requires several days. Presumably in normal women modification occurs about the time of menstruation. We cannot rule out the possibility, however, that the differing conditions of ovariectomized and normal women may cause a variation in the effect of the combined hormones.

### Summary

The skin of trunk and limbs of three ovariectomized and five normal young women was studied with the Hardy recording spectrophotometer. In both groups of subjects the pigments of the skin were unchanged excepting reduced

hemoglobin and oxyhemoglobin. Results in the hands and feet were inconclusive, and the face was not studied.

After ovariectomy, the sexual characteristics of the female skin do not disappear, suggesting a genic control. A diminution in vascularity is noted, evidenced by lowering of the amount of hemoglobin with a relative preponderance of the reduced form. Administration of estrogen was followed by an increased cutaneous blood flow with an actual increase in oxyhemoglobin. Progestin markedly increased the proportion of oxyhemoglobin, but did not consistently increase the total hemoglobin. The combined administration of both hormones results in a diminution in hemoglobin with a predominance of the reduced form.

In the early part of the normal cycle, the curves resemble those obtained from ovariectomized subjects. After mid-cycle, there is evidence of greatly increased vascularity which reaches a maximum in the premenstrual period. This is consistent with the observed effects of the two hormones acting in the latter half of the cycle, since previous workers have shown that progestin takes several days to modify estrogen effect.

Unlike the situation in many other mammals, in which reactivity to the female sex hormones is localized in special areas, the human skin probably reacts in its entirety.

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## CHANGING CONCEPTS OF X-RAY PELVIMETRY\*

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THE use of x-ray has given impetus to the study of pelvimetry and the female pelvis, resulting in the development of many techniques. We desire to review the changing concepts of x-ray mensuration, discuss its related problems, and suggest a solution.

### X-Ray Measuring Devices (Fig. 1)

The Thoms<sup>13</sup> technique uses a very large appliance with a perforated centimeter grid for measuring chiefly the inlet. The patient must be removed from the table for the second lateral exposure.

Javert and Steele<sup>7</sup> developed a modification of the Thoms, combining a notched centimeter ruler with a distorted scale as a final measuring device, and used the precision stereoscopic method developed by Caldwell, Moloy, and Swenson.<sup>2</sup> This latter technique, elaborated by Swenson with stereoscopic and lateral films, constitutes a very complete study.

The Ball<sup>1</sup> calculator is an empirical volumetric examination with construction of a sphere from the diameters.

The Snow-Lewis<sup>11</sup> Slide Ruler by geometric formula can solve the original object diameter. Many calculations are necessary.

In the method developed by the authors,<sup>3</sup> a rotating ruler with centimeter perforations is placed beside the body in both the anteroposterior and lateral positions taken at approximate right angles to each other at any distance. Direct readings are made on each film.

Any of these devices and many others long in use by the radiologist should give accurate results. Therefore, accuracy in pelvimetry is not a problem.

### Diameters of the Pelvis

No attempt will be made to discuss in detail all the suggested diameters of the pelvis (Fig. 2). There are many of them from the inner sacrum to the inner symphysis. Of the true pelvis alone, there are at least twenty suggested diameters, but only the more recent concepts will be discussed.

The coccyx may be eliminated as a criterion for measuring diameters. Newer concepts indicate that it is not as important as it seems, because it is a mobile unit and presents no real obstacle, unless it is fixed or abnormally large and forward.

The true conjugate diameter has no corresponding transverse diameter, and is well above the brim of the true pelvis. The literature tends to show that the so-called conjugata vera is not a critical factor in the progress of labor. Since the conjugata vera is in the false pelvis, it could be named more properly the "false conjugate."

Let us evaluate the diameters of the true pelvis. The drawings in Fig. 1 show some of the various diameters of the pelvis. Thoms,<sup>13</sup> Javert and Steele,<sup>7</sup> and Ball<sup>1</sup> do not indicate any particular relationship between their anteroposterior and transverse diameters.

Snow and Lewis<sup>11</sup> form a three-level pattern with their transverse diameters. The inlet is formed by its greatest transverse diameter, the midpelvis between the spines of the ischium, and the outlet between the tuberosities of the ischium. These diameters are also used by the authors.

\*Presented at a meeting of the Philadelphia Obstetrical Society, Jan. 8, 1948.



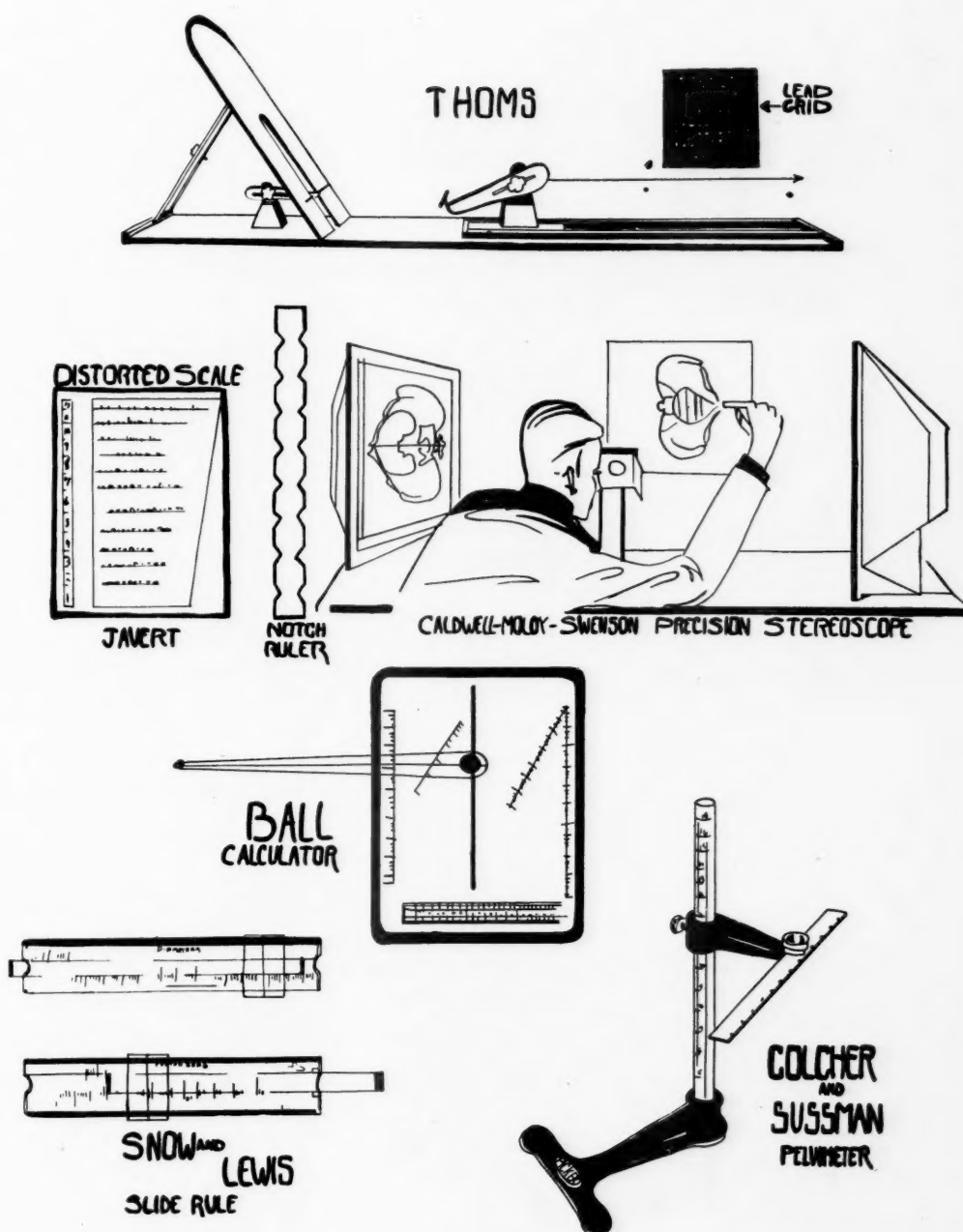


Fig. 1.—X-ray pelvimetry devices.

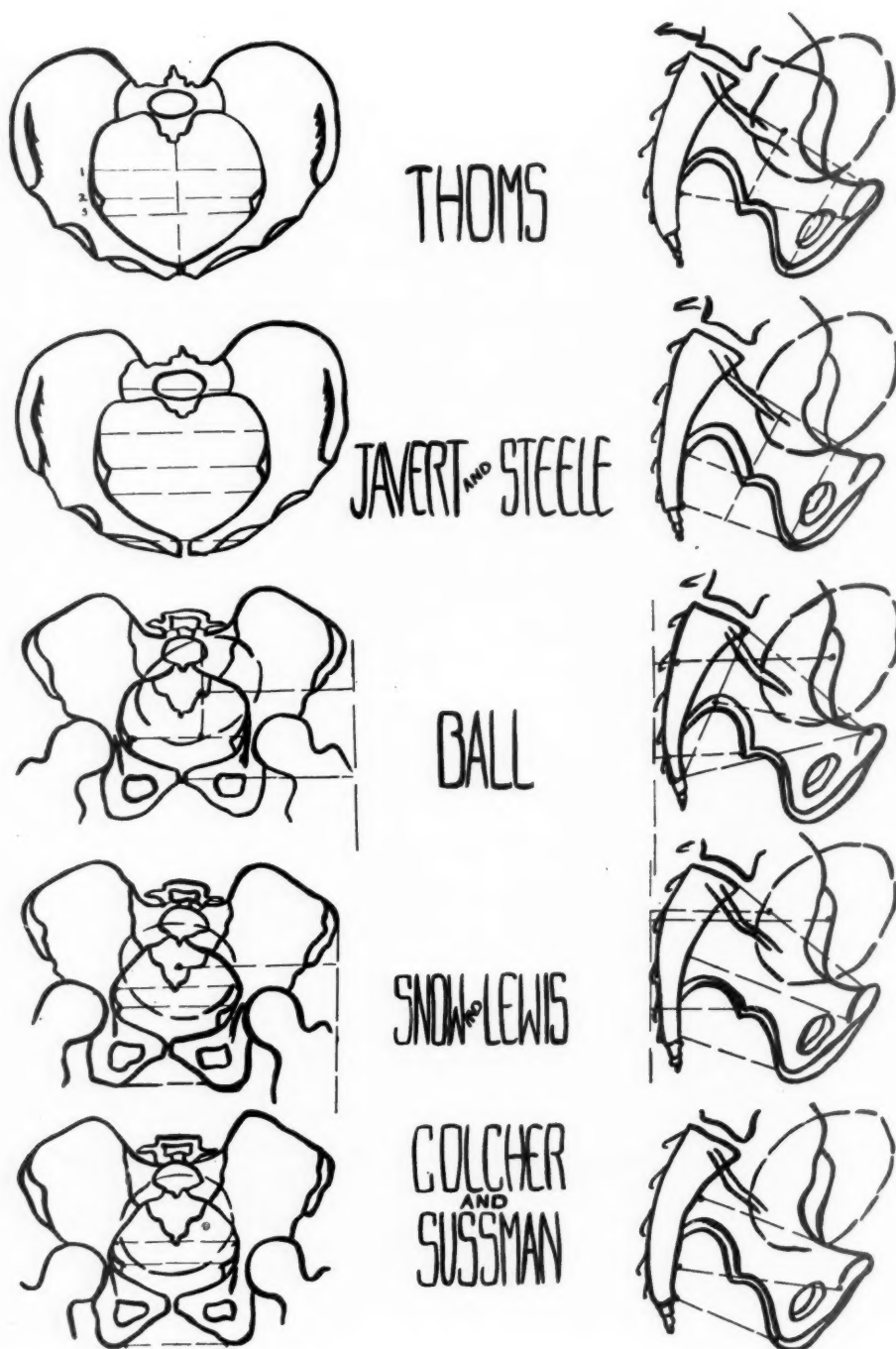
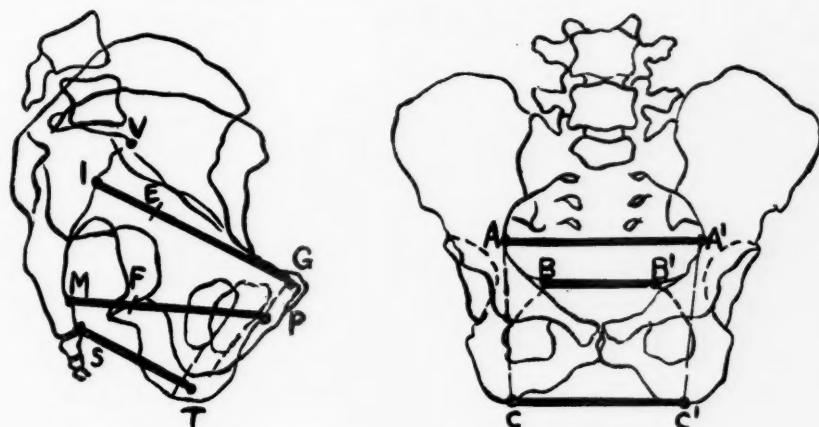
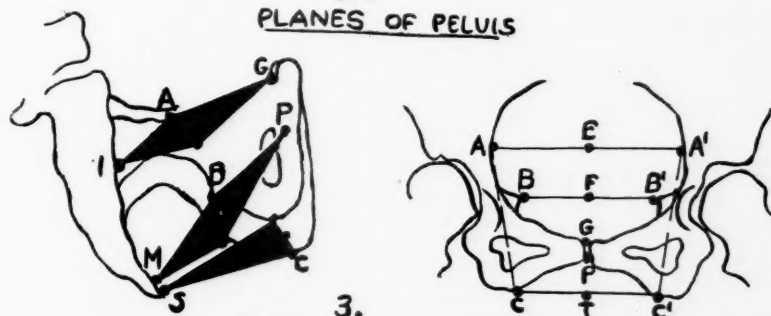


Fig. 2.—Pelvic diameters.

1.  
INTERSECTING DIAMETERS OF PELVIS



2.  
PLANES OF PELVIS



3.  
TRIANGLES OF PELVIS

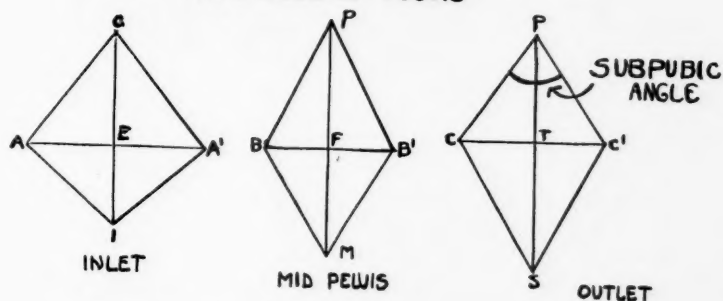


Fig. 3.—1. Intersecting diameters of the inlet, midpelvis and outlet.  
2. Perspective view of the three planes of the true pelvis, including the intersecting diameters. The subpubic angle is C-P-C'.  
3. The triangles of the pelvis with both the anterior and posterior segments may be reproduced in life size with the same films.

Concerning the anteroposterior diameters, Ball<sup>1</sup> and Lewis<sup>11</sup> continue to use the conjugata vera, whereas Thoms<sup>13</sup> and Javert and Steele<sup>7</sup> have now discarded the conjugata vera and move down toward the true pelvis for the obstetric conjugate. This conjugate is at the brim of the pelvis. The authors move into the true pelvis and utilize the level of the transverse diameter of the inlet which on the film is located about midway between the brim of the pelvis and the sacrosciatic notch. A line is drawn from the upper symphysis through the inlet diameter and extended to the sacrum, completing the diameters of the inlet. These intersecting diameters, previously described by the authors (Fig. 3),<sup>4</sup> may now form a plane completing the first bony ring of the true pelvis through which the fetal head must pass. The actual inlet can thus be divided into anterior and posterior segments.

To continue this pattern, the midpelvic plane is drawn from the lower symphysis through the middle of the transverse ischial diameter and extended to the sacrum. This also forms a plane and creates both anterior and posterior segments. The outlet plane, between the tuberosities of the ischium and the tip of the sacrum, now forms the posterior segment or triangle of the outlet. This triangle has additional space forward under the subpubic arch. With this technique, all the salient bony factors of the true pelvis are utilized. Any one segment can be individually measured directly from the film.

### Positioning of the Patient for Pelvimetry

Concerning the position of the patient for the anteroposterior diameters (Fig. 3),<sup>3</sup> the lateral view has definitely been standardized. The patient lies on her side, and the ruler, with centimeter markings, is placed at the midsacrum. The distortion of the diameters is the same as that shown by the ruler, and direct readings can be made. This method justly enjoys popular usage and is invaluable in x-ray pelvimetry. Erect films may also be made in like manner.

In positioning for the transverse diameters (Fig. 5), Thoms<sup>14</sup> has the patient reclining at an angle on a special apparatus. This position elevates the sacrum, lowers the forepelvis, and allows direct visualization of the contour of the inlet. With the patient recumbent and with various-sized pads placed under the back, Javert and Steele,<sup>7</sup> Snow and Lewis,<sup>11</sup> and Ball<sup>1</sup> show a gradual lowering of the back with a gradual elevation of the forepelvis. In our technique (Fig. 4b),<sup>3</sup> the knees are flexed, the spine is flat, and greatest elevation of the forepelvis is attained; the midpoints of the inlet, the spines of the ischium (midpelvis), and the tuberosities of the ischium (outlet) are on the same plane in relation to the tabletop and, thus, on the same level with the film placed in the x-ray table. By placing a centimeter ruler at the level of the tuberosity of the ischium, all the transverse diameters are measured directly on the film with the same distortion as that on the ruler. *The very same technical factors for measuring the pelvis in the lateral view are now possible in our anteroposterior positioning.*

When the head is the presenting part, the fetal head diameters are also measured with the same ruler. While the over-all measurements of the fetal head should be considered, we believe that the suboccipito-bregmatic and biparietal diameters are of greater importance. A table gives the subpubic angle in degrees.

### Practical X-ray Evaluations

The number of x-ray pelvimetric methods published emphasizes and justifies its use in obstetrics. We believe that it has definitely been shown that the external measurements and maneuvers of a physical examination are not only



unsatisfactory but questionable as to accuracy. For instance, J. T. Williams,<sup>15</sup> after examining externally 300 primiparas, found that many with broad hips and large external measurements had contracted outlets and narrowed subpubic angles, while many of those with narrow hips had broad outlets with ample transverse diameters of the outlet and wide subpubic angles. Jarcho<sup>6</sup> states that most estimates of the size of the pelvic inlet, when done by physical examination, are inexact and unreliable. Thoms<sup>14</sup> says that the most careful external measurements are unreliable. According to Rohan Williams,<sup>16</sup> the possible disproportion between the head and the pelvis is one of the most difficult things to determine in obstetrics, and he concludes that clinical measurement of the true conjugate is either impossible or inaccurate, except in cases of severe pelvic contraction. By the same token, these men indicate that only by proper x-ray pelvimetry can an accurate determination of the necessary factors of the pelvis and fetal head be made possible.

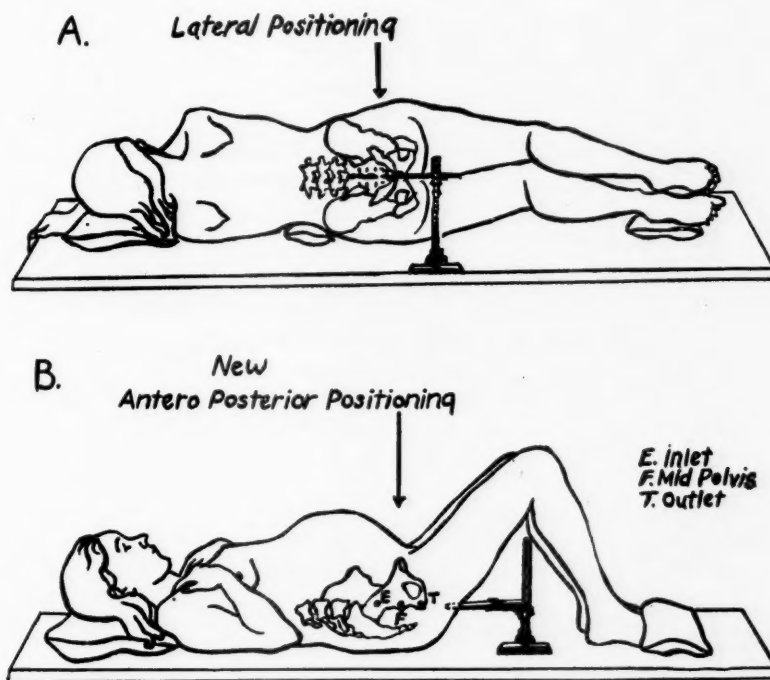


Fig. 4.—A. X-ray position for the lateral view with the centimeter ruler at the mid-sacrum.

B. New positioning for the anteroposterior film with the centimeter ruler at the level of the tuberosity of the sacrum (T). Midpelvis at spines of ischium (F), and inlet at (E) are all on the same level.

Stander,<sup>12</sup> in his recent book, says, "I believe the reduction in fetal mortality from 3.6 per cent in 1932 to 2.2 per cent in 1943 is in part due to the integration between clinical and x-ray pelvimetries." Thoms<sup>14</sup> x-rayed 1,100 primiparas with only 2.3 per cent cesarean sections.

For many years, one of us (Sussman) has been educating his patients for x-ray pelvimetry. Various techniques were used until the evolution of our technique with a series of 450 cases since 1943. These included routine studies of all primiparas and multiparas with previous history of difficult labors. The films were taken about ten days before term. The most troublesome question

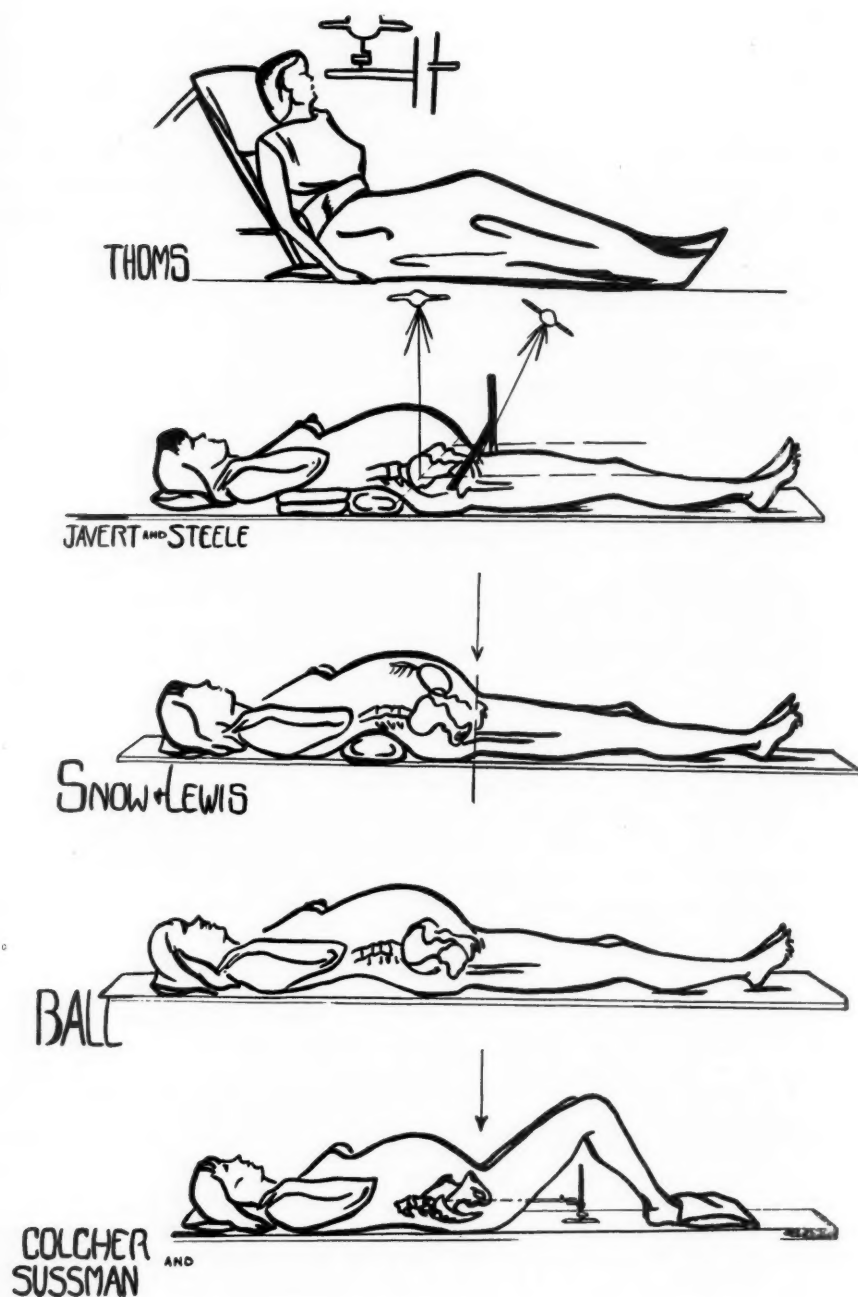


Fig. 5.—Various positions for anteroposterior films.

was the use of emergency x-ray outside of technical working hours. Cumbersome technique and difficulty in reading the films were also obstacles. With our present method, the obstetrician can easily learn to read his own films and correlate this with his clinical art. Our cesarean section rate (uncorrected) from 1943 to, and including, 1946 was 6 per cent, and in 1947, 3.7 per cent. We had five patients delivered per vagina who had had previous cesarean sections. No babies were lost due to cephalopelvic disproportion.

### Conclusions

While our series of 450 cases is not large, our statistics, as well as the cases mentioned, tend to show a decrease in the incidence of cesarean section in cephalopelvic disproportion and a decrease in fetal mortality. And yet the radiologist seems to avoid this type of examination. Why, with all its advantages, is x-ray pelvimetry not more popular? The reason, we believe, is self-evident. Despite the driving interest in this type of investigation—from Granzow,<sup>5</sup> who first introduced a measuring ruler, to the present time (about 422 articles on pelvimetry in the last 18 years)—and the innumerable measuring improvements devised, the x-ray reports and interpretations remain confusing. An obstetrician who has several hospital connections may find that each hospital will use a different technique, different diameters, and different elements of evaluation. As a result, the practical values are obscured.

No universal language or technique is at present employed wherein radiologists and obstetricians may use the same terms and make like interpretations. A similar situation was recognized almost half a century ago when the American Gynecological Society, in 1905, appointed a committee, Drs. King, Williams, and Davis,<sup>8</sup> for this purpose, and a series of compromise diameters and measurements was published and accepted. There were thirteen diameters at that time. Today there are many more, with one author stressing his own concept of the proper diameters, and another stressing his apparatus and technique, all of which results in confusion.

It would, therefore, seem timely to consider means of formulating standards for a universal technique and terminology.

We have made an effort to describe the changing concepts in x-ray pelvimetry, and suggest that one of the techniques should be accepted and that it should be simple and concise enough to be accurate in the hands of both the radiologist and obstetrician.

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### Discussion

DR. PAUL C. SWENSON.—During the past five years I have combined the method of pelvic measurement by these authors with stereoscopic films and have been able to obtain equally good studies of the female pelvis as I did with the precision stereoscopic means alone. In fact, the method has proved to be easier and less expensive as well.

Drs. Colcher and Sussman should be congratulated on having called our attention to the necessity for unanimity of thought, if not technique, as far as x-ray methods are concerned in obstetrics. It is obvious that the mere mensuration and typing is not the important thing. We must have a standardization of thought as well as a means of mensuration. The actual measurements are not the important thing. Any method well done can be developed to a sufficiently accurate stage in anyone's hands, but the proper approach, interpretation, and correlation of clinical findings are important.

The essayists would like to have some sort of standard terminology applied to mensuration. This is commendable. We have several indices of size and disproportion which seem to work out well in any one individual's hands, but not in others. The difficulty is that no hard and fast rule can ever be made. I have seen exceptions to all rules and therein lies the danger of certain hard and fast indices. The over-all picture must always be kept in mind.

At the present time, our chief difficulty has been in trying to measure the fetal head accurately in order to estimate the fetal weight. I have not been able to be certain of this procedure at all, no matter how accurate I try to be using the methods of Snow and Ball. I find that there are just too many variables. This is in agreement with the findings of others. Donaldson of Ann Arbor, for example, has recently checked several methods in a large number of cases and finds that he can be accurate within one-half pound in only one-third of the cases. To those, therefore, who look for the last word in these methods of mensuration, I give only a word of warning that they are fooling themselves since too much reliance is placed on these procedures alone. They are important, but not the whole story.

I always like to think of the words of DeLee who, after warning of all the pitfalls in pelvimetry alone, immediately follows this by the remark that he would, nevertheless, not be without pelvimetry, but the findings should always be taken in conjunction with the clinical situation.

With regard to the level of the true conjugate, it was Caldwell's considered opinion that because, in the usual case, the symphysis was below the level of the promontory and therefore in a different plane, the diameter past which the fetal head had to pass when engaged by both the anterior and posterior bony limits was definitely lower than it was usually thought to be. It usually falls along the iliopectineal line. This particular point was determined by following cases through labor with films at varying intervals, thereby watching the adaptation of the fetal head to the inlet.

I did not mean to imply in my first discussion that there was any difficulty in interpreting the diameters as we measure them, but rather that when we have these various diameters measured it becomes difficult to make anything out of the data at all, if one does not individualize each case and discuss it with the obstetrician, for a correlation with the known clinical background. If one does not do this, one might just as well discard the x-ray evidence. I think we are all agreed that in many cases pelviography is a very important adjunct, but I think it can be stated without argument that the negative evidence is perhaps the most important; that is to say, if a well-formed, roomy, and adequate pelvis is found with an average-sized fetus, there is one cause for dystocia which can be eliminated; namely, bony obstruction. Therein lies 90 per cent of the value of the examination. When, however, there is borderline disproportion, the measurements become of less importance. The clinical background, the fetal pelvic relationships, and the pelvic type then are of greater importance in the management of the individual case.

DR. A. E. SCHUMANN.—I have on many occasions enjoyed watching the stereoscopic progress of labor as demonstrated by Dr. Caldwell and was delighted and amazed by the



ability to demonstrate the mechanism of labor. I am forced to the conclusion that x-ray pelvimetry is quite difficult. I would even venture to disagree with Swenson. I do not think this subject too important. Though the authors do not seem to think the promontory is of any importance, I seem to remember cases of many fetal heads that failed to get beyond that level. Obstetricians should make the textbook of Hugh L. Hodge, in which the pelvic planes are described, required reading. I do know that by the Thoms technique it is perfectly possible to measure the size of the pelvic inlet laterally and posteriorly within 2 mm. of the actual measurement. We did an interesting experiment in Kensington Hospital some years ago. Two hundred gynecologic cases were subjected to a special study and when the patient went to the operating room accurate measurements were made and recorded on the operation sheet. When the patient was convalescing from the operation, she was x-rayed by the Thoms technique. She was then subjected to external pelvic measuring and that was recorded on a separate sheet and we then reviewed her obstetric history, if any. When these factors were all assembled as to patients, we found that the obstetric history as related to pelvic measurements, whether x-ray or other method, was singularly variable. Women who we thought would have difficulty delivered spontaneously and the capacious pelvis frequently had required cesarean section. We found external pelvimetry bore no relation to the actual size of the pelvis. In particular, the most disappointing was the diameter of Baudelocque. We did find in all our cases the measurement by the technique of Thoms when compared with the actual measurement in the open abdomen was accurate to within 2 mm. To me, if I am given the size of the pelvic inlet and its shape, I am not much concerned about any other measurement of the pelvis unless it is curiously deformed. Given the size and shape of the inlet and the other factors of the quality of uterine contractions, size of head, and presentation of the head, I think it is only pelvic diameter that is required and that only that is of any service. The Ball technique has been a notable failure in my experience.

DR. SUSSMAN (Closing).—In the literature the term cephalopelvic disproportion is defined as dystocia, including bony and soft tissues. In this paper we define it sharply as a true disproportion between the bony presenting part and the actual bony pelvic structures.

Dr. Swenson states that about 2 per cent of obstetric cases fall within the disproportion group. Dr. Thaddeus Montgomery, in a cesarean survey, found that about 42 per cent were done for cephalopelvic disproportion. More recently, Andrews, Nicholls, and Andrews found their statistics showed almost 50 per cent.

We know that x-ray films do not permit guessing. All available facts are in the obstetrician's hands. The obstetrician should go over the films and correlate the findings with his clinical observations. In our series of approximately 450 cases, we have cut our cesarean rate to 25 per cent. We have lost no mothers or babies due to true cephalopelvic bony disproportion.

We suggest that the obstetrician should know all the facts. We plead for a universal nomenclature. We know that the maternal and fetal morbidity and mortality will be astonishingly low if you take care of the complicated 2 per cent of cases. Only by routine x-ray pelvimetry can you save life and avoid disability.

DR. COLCHER (Closing).—Dr. Montgomery brings up an important issue concerning the value of the true conjugate and obstetric conjugate versus the authors' actual inlet. We have shown, on dried specimens of the pelvis of the young female, that the actual inlet is the first complete bony ring through which the fetal head must pass before a delivery is possible. This inlet is usually well below the promontory of the sacrum, and lies on a level with the greater transverse diameter of the inlet. Thus, a fetal head may pass through a narrow true conjugate, like a rubber ball passing between two points, but will encounter great difficulty in passing through a constricted circle of bone. That is the basis for the new location of the actual inlet.

Dr. Schumann believes the inlet is important, and Dr. Montgomery indicates the inlet and outlet as important. We believe the obstetrician should be fully informed on all measurements and diameters, and utilize what he deems important in that particular instance.

Finally, to obtain good results, there must be cooperation between the radiologist and obstetrician. Otherwise, the value of pelvimetry becomes questionable.

## EXTRAPERITONEAL CESAREAN SECTION IN THE PROFOUNDLY INFECTED PATIENT\*

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ONE of the advances in modern obstetrics has been the simplification and clarification of techniques for extraperitoneal cesarean section. Though Sellheim, Frank, Latzko and others might be mentioned as leading figures in the development of this operative approach, Waters<sup>1, 2</sup> and Norton<sup>3</sup> have added to the recent refinement of this type of cesarean section and, in their large series of cases, have shown this approach to be practical, safe, and within the technical skill of the trained obstetric surgeon.

However, as sometimes is seen during the development of a new approach to a problem of long standing, this technique has not everywhere met with praise. In fact in some quarters its use is severely denounced. It would seem that there has risen a difference of opinion over the general efficacy of and indications for this procedure which threatens to develop into a controversy as bitter as that of a few years ago between classical and low cervical cesarean section.

It has been estimated in recent years that at least 38 per cent of all cesarean section deaths are due to infection.<sup>4</sup> The majority of these are due to peritonitis<sup>5</sup> and follow operations of the transperitoneal type. These usually have been done upon patients who have had long labors, with ruptured membranes for a considerable period, or upon whom there have been frequent vaginal examinations or attempts at delivery. It is, therefore, quite evident that we are, at the present time, faced with the problem of improving this regrettable situation. We may hope that methods which will more positively diagnose the state of the pelvis, the pliability of the soft parts, and the more exact potentialities of the uterine musculature to contract normally and vigorously may be developed in the future to help prevent such things from happening. In the meantime, however, while we are working toward this end, the stark reality remains that we are occasionally bound to be confronted with such badly infected cases.

The fact that each succeeding hour of labor, ruptured membranes, or a combination of the two increases the probability of intrauterine infection has caused modern clinics to attempt to manage cases with this in mind. Certain rules are set up which preclude further procrastination after a certain interval and often dictate the procedure allowed for delivery after a predestined deadline of time has been reached. An excellent example of such a set of standards is that followed by Dieckmann<sup>6</sup> at the Chicago Lying-in Hospital. He lists the following as contraindications to transperitoneal cesarean section:

\*Read at a meeting of the Philadelphia Obstetrical Society on Jan. 8, 1948.

1. Labor over twenty-four hours
2. Ruptured membranes over twenty-four hours
3. Attempts at delivery by forceps or version
4. Induction of labor by bag, bougie, or pack
5. Evidence of uterine infection
6. More than six vaginal examinations
7. More than twelve rectal examinations
8. Dead or damaged fetus

Few would disagree with many of these contraindications, but there is definitely a divided opinion as to how to manage patients who have gone beyond the criteria mentioned. Dieckmann<sup>6</sup> states that such patients should be treated by embryotomy or cesarean hysterectomy when normal vaginal delivery is not possible. The proponents of extraperitoneal cesarean section state that this approach was devised in order to allow suprapubic delivery in infected cases, such as violate these criteria, without possible soiling of the peritoneal cavity and subsequent development of peritonitis. This division of opinion regarding cesarean hysterectomy, embryotomy, extraperitoneal cesarean section, and possibly transperitoneal section with large doses of antibiotics and chemotherapy has prompted the author to review the results obtained in such cases when treated by extraperitoneal technique.

Three personal series of consecutive cases of extraperitoneal cesarean section done in Philadelphia within the last few years were reviewed. It was found that the majority of operations were done upon patients after several or all of the criteria set by Dieckmann had been violated.

TABLE I

TOTAL CASES		EXCEEDING CRITERIA	FETAL MORTALITY	MATERNAL MORTALITY
Paxson	20	9	0	0
Briscoe <sup>7</sup>	37	30	5	0
McCall	34	25	3	0
Totals	91	64	8	0

There was no maternal mortality. The fetal mortality was 8.8 per cent, and 9.4 per cent of the cases exceeding the criteria had babies who died of infection or the result of prolonged labor.

In the group of cases exceeding the criteria, it was evident that there were some patients who were extremely ill from the effect of far-advanced intra-uterine infection. Rather than dwell upon the over-all picture of extraperitoneal section and technique, it was thought that a more critical résumé of these badly infected cases would be more significant, since such cases present the most adverse conditions with which to test any procedure used in treatment.

### Case Reports

CASE 1.—(Philadelphia General Hospital.) A 29-year-old Negro, gravida i, para 0, at term, was first seen after 99 hours of labor and 33½ hours of ruptured membranes. She was very toxic and psychotic with a fever of 103° F. and pulse of 170. Labor pains were five minutes apart and the uterus was tense and tender. Fetal heart tones were still present. The baby, in left occipitoposterior position, had a greatly molded head extending down to

within 1 cm. of the ischial spines. The cervix was half effaced and 4 cm. dilated. The clinical measurements of the pelvis were small but upon x-ray done earlier there was no report of disproportion.

Penicillin and sulfadiazine had been started a few hours earlier. An extraperitoneal cesarean section was performed under continuous spinal anesthesia. The uterus was filled with foul-smelling pus and its wall was gray and necrotic for a depth of about one-fourth inch. The child, a 7 pound, 2¼ ounce boy, was living and recovered uneventfully, although it carried with it a foul odor for several days and was given penicillin. The patient was quite ill for three days postoperatively but developed no sign of peritonitis. There was a low-grade fever for twelve days and the incision drained for eight days. The highest temperature after operation was 102.8° F. She was discharged in good condition on the 20th postoperative day.

CASE 2.—(Philadelphia General Hospital.) A 36-year-old Negro, para 0, gravida ii, at term, was first seen after over 60 hours of labor and 53 hours of ruptured membranes. She appeared to be at the point of death with a fever of 103.4° F. and a poor pulse of 170. She was toxic and psychotic, respirations were irregular, and there were many râles at the lung bases. The uterus was very tense and tender, although there were still irregular uterine contractions. No fetal heart sounds were heard. Examination revealed a vertex presentation in right occipitoposterior position at minus one station. The cervix was partially effaced and 3 cm. dilated. Clinical measurements showed outlet to be contracted. Penicillin had been given for twenty-four hours before the patient suddenly became critically ill. After some supportive preoperative care, an extraperitoneal section was done under local anesthesia and a 7 pound, 15 ounce stillborn boy delivered. The uterus contained a large amount of foul-smelling pus which was under such pressure that it spurted several feet when incised. The uterine lining was gray and necrotic. Cultures revealed *Streptococcus hemolyticus*, *Staphylococcus aureus*, and *Bacillus coli*. The patient's condition improved from the moment the uterus was evacuated. The highest temperature postoperatively was 103.4° F., although there was a low-grade fever for fifteen days and drainage from the wound for sixteen days. A transient mild thrombophlebitis responded to conservative therapy. She was discharged in good condition on eighteenth postoperative day.

CASE 3.—(Philadelphia General Hospital.) A 30-year-old Negro, gravida i, para 0, at term, was first seen after 168 hours of labor and 240 hours of ruptured membranes. She had a borderline pelvis and secondary uterine inertia. Her temperature was 102.4° F. This had been preceded by a chill and a temperature of 106° F. Adequate doses of sulfadiazine had been given for over 48 hours and penicillin for 24 hours before the patient became critically ill from infection. The pulse was 130. The uterus was tense and tender and there was a foul vaginal discharge. Examination revealed the vertex molded to within 1 cm. of the spines. The cervix was 3 cm. dilated and partially effaced. An extraperitoneal section was done under continuous spinal anesthesia and an 8 pound stillborn infant delivered from the pus-filled necrosis-lined uterus. The highest temperature postoperatively was 102.4° F., but there was a low-grade fever for ten days. The wound drained for eight days. She was discharged in good condition on the sixteenth postoperative day.

CASE 4.—(Episcopal Hospital.) A 24-year-old, white, gravida i, para 0, at term, was seen after 100 hours of labor and 60 hours of ruptured membranes. The patient was weak and acutely ill with a temperature of 101.4° F. and pulse of 124. There was mild tenderness of the uterus and a foul vaginal discharge. Examination revealed cephalopelvic disproportion and the head was greatly molded. The cervix was 4 cm. dilated and partially effaced. There was secondary uterine inertia. An extraperitoneal cesarean section was done under continuous spinal anesthesia and a living full-term male infant delivered. The uterus contained pus which showed a pure culture of *Hemophilis influenzae*. The highest temperature postoperatively was 103° F. and there was a low-grade fever for five days, with only mild drainage for five days. She was discharged in good condition on the twelfth postoperative day.



CASE 5.—(Philadelphia General Hospital.) A 33-year-old Negro, gravida i, para 0, at term, was seen after 120 hours of labor and 105 hours of ruptured membranes. She had a temperature of 102° F., with a pulse rate of 120. Intrauterine death had taken place several days before and because clinical measurements and x-ray showed no disproportion, spontaneous delivery had been contemplated. In spite of penicillin therapy for 48 hours, the patient became critically ill with signs of intrauterine infection. The vertex was at zero and the thick cervix was only 2 cm. dilated. The uterus was tense and discharge foul. An extraperitoneal cesarean section was done under continuous spinal anesthesia and an 8 pound, 3 ounce stillborn macerated male child removed from the pus-filled uterus. The highest temperature postoperatively was 103° F. and there were five days of low-grade fever. There was drainage from the drain area in the incision for seven days. The patient was discharged in good condition on tenth postoperative day.

CASE 6.—(Philadelphia General Hospital.) A 33-year-old Negro, gravida i, para 0, at term, was seen after 108 hours of labor and 65 hours of ruptured membranes. Examination revealed a very tired patient with a temperature of 100.4° F. and pulse 110. The uterus was tender. Fetal heart sounds were present and there was a foul vaginal discharge. X-ray revealed an android type pelvis. The unengaged head was jammed into the superior strait and the caput extended to within 1 cm. of the spines. The cervix was 5 cm. dilated and 50 per cent effaced. An extraperitoneal cesarean section was done under continuous spinal anesthesia. The amniotic fluid was foul and thick. A living girl, weighing 5 pounds, 13½ ounces was delivered. The postoperative course was uneventful, the highest temperature being 100.4° F. Patient was discharged in good condition on thirteenth postoperative day.

CASE 7.—(Episcopal Hospital.) A 40-year-old white woman, gravida iii, para i, at 32 weeks' gestation, was seen after 100 hours of ruptured membranes. There were no pains. The first pregnancy had been terminated with high forceps after accouchement forcé and the fetus was stillborn. This was followed by a trachelorrhaphy because of residual cervical pathology. The second pregnancy was terminated in much the same manner with the aid of Dührssen's incisions after premature rupture of the membranes. This child was living but had been mentally inferior. In the present pregnancy, after rupture of the membranes, several medical inductions had failed. These were followed by four vaginal examinations with some manipulation of the cervix. When seen by the operator there was a foul vaginal discharge, a floating premature breech with heart tones present and no dilatation of a scarred cervix. There was a temperature of 100° F. and pulse 108. The uterus was slightly tender and the patient had suddenly become quite weak and languorous. An extraperitoneal cesarean section was done under continuous spinal anesthesia and a 4 pound 12½ ounce normal living girl delivered. The amniotic fluid was thin but very foul in odor. The highest temperature postoperatively was 101° F. and there was low-grade fever for five days. Patient was discharged in good condition on the thirteenth postoperative day.

CASE 8.—(Episcopal Hospital.) A 33-year-old white, gravida i, para 0, at term, was seen after 25 hours of labor and ruptured membranes for 72 hours. Left occipitoposterior at zero station with 4 cm. dilatation of a thick cervix. The patient was tired and toxic and the uterus was tense and tender. Examination revealed a funnel pelvis with contracted outlet. Temperature was 100.4° F. and pulse 104. A foul purulent vaginal discharge was evident. Under continuous spinal anesthesia an extraperitoneal section was done and a living full-term child delivered. The amniotic fluid was thick and gave forth an offensive odor. The highest temperature post partum was 101.4° F. There was purulent drainage from the lower angle of the incision for six days. She was discharged in good condition on eleventh postoperative day. Twenty-one months later a second child was delivered by elective cesarean section.

CASE 9.—(Jefferson Hospital.) A 26-year-old Negro, gravida i, para 0, at term, entered hospital in labor after membranes had ruptured at home three and one-half days before.

After a total of 30 hours' labor and 100 hours ruptured membranes, a temperature of 101.4° F. developed, with a pulse of 130. The patient was toxic and obviously infected, with a tender uterus and foul vaginal discharge. Left occipitoanterior at minus one station with cervix 3 cm. dilated. X-ray showed much molding of head without engagement. Extraperitoneal section was done under continuous spinal anesthesia. The lower uterine segment was so thin that it ruptured during the usual retraction. The amniotic fluid was foul and under pressure. A normal full-term male child was delivered. The temperature became normal on the fifth day and there was no further draining from the lower angle of the incision after that time. She was discharged in good condition on the eleventh postoperative day.

CASE 10.—(Philadelphia General Hospital.) A 17-year-old Negro, gravida i, para 0, at 39 weeks' gestation, was seen after 87 hours of labor and 86 hours of ruptured membranes. The head had rotated completely posterior and was markedly molded in a small pelvis. The vertex extended 1 or 2 cm. below the spines. The cervix was thick and only 3 cm. dilated. Vaginal manipulation with attempt at manual dilatation and rotation has been done. The patient was ill and weak. The uterus was tense and tender. There was secondary uterine inertia and a purulent malodorous vaginal discharge. Penicillin had been given in adequate dosage for 72 hours but the patient was rapidly becoming increasingly toxic with signs of uterine infection. The temperature at the time of operation was 100.2° F. Extraperitoneal section under continuous spinal anesthesia was performed. A living 5 pound, 12 ounce girl was delivered. The fever went no higher and there was an uneventful recovery. Discharged on tenth postoperative day.

CASE 11.—(Philadelphia General Hospital.) A 23-year-old white, gravida i, para 0, at term, was placed in a room adjacent to her physician's office during the early part of labor. While there she was frequently examined vaginally by the doctor who, according to the patient, never wore gloves and always washed his hands afterward, not before. After twenty-four hours of labor, the patient was anesthetized and a version attempted, which failed. Several attempts were then made to deliver her with forceps but these kept slipping off. An ambulance was called and she was taken to the hospital in shock, undelivered. In the hospital, with the aid of transfusions and other supportive therapy, her condition improved. Examination revealed the baby to be in brow presentation, the head floating. Fetal heart sounds were not heard. The cervix was not completely dilated and there was a foul discharge. The pelvis was contracted. A complete tear was present through the sphincter of the anus into the rectum. There was also perforation in the bladder just below the urethra. This was closed and an extraperitoneal section done under continuous spinal anesthesia, the patient's general condition having revived remarkably. A 6 pound 1 ounce stillborn male with multiple skull fractures was delivered. The amniotic fluid had a foul odor. The third degree tear was also repaired. The patient responded very well. The highest temperature was 102° F., although there was some low-grade fever for seven days and some drainage from the incision for five days. Discharged on sixteenth postoperative day. There have been two subsequent operations for repair of the vesicovaginal fistula. The last one was successful.

CASE 12.—(Pennsylvania Hospital.) A 37-year-old white, gravida vi, para iv, at term. Had small babies in the past. After 60 hours of labor and 48 hours of ruptured membranes, the head was not engaged but was molded tightly into the upper pelvis with over-riding at the symphysis, 8 cm. dilatation of the cervix. High forceps were attempted but failed. There was a temperature of 100° F. and pulse of 110. An extraperitoneal cesarean section was done under continuous spinal anesthesia and an 8 pound 5 ounce female infant, which died shortly thereafter, was delivered. The postoperative course was hectic and there was fever for thirty-six days, the highest level being 104.8° F. There was evidence of bilateral pelvic thrombophlebitis during this time. The patient recovered and was discharged on the forty-eighth day following her operation.

CASE 13.—(Pennsylvania Hospital.) A 31-year-old white, gravida i, para 0, was seen after 44 hours of labor and 34 hours of ruptured membranes. The patient was ill from the toxemia of infection. The uterus was tense and tender. There was a putrid vaginal discharge. The head was not engaged and there was obvious cephalopelvic disproportion. Temperature was 101.4° F., pulse 112. Extraperitoneal section was done under continuous spinal and a 6 pound 1 ounce normal living male infant delivered. The patient responded well after this, but developed wound infection with a temperature of 102° F. for three days. Discharged on fourteenth postoperative day.

CASE 14.—(Pennsylvania Hospital.) A 29-year-old white, gravida i, para 0, at term, was seen after an attempt to deliver by high midforceps had failed. She had been in labor 58 hours with ruptured membranes for 68 hours. The cervix was almost completely dilated. The abdomen was tender over the uterus and quite tense. A large baby was present and the fetal heart tones were still present. There was a malodorous purulent vaginal discharge and the patient appeared to be ill and toxic from infection. The temperature was 101° F. and the pulse 124. A 9 pound 8 ounce normal living female infant was delivered by extraperitoneal cesarean section under continuous spinal anesthesia. The patient responded well after operation and the highest temperature was 102.4° F. There was a temperature between 99° and 100° F. for ten days postoperatively. Discharged on eleventh postoperative day in good condition.

CASE 15.—(Pennsylvania Hospital.) A 21-year-old white, gravida i, para 0, at term, with a border-line pelvis, had had an attempted delivery with midforceps, which failed. She had been in labor for 50 hours with ruptured membranes. The vertex was at zero station and there was a rim of cervix remaining. The temperature was 101.4° F. and pulse 122. There was a foul vaginal discharge and the patient was worn out. A normal full-term child was delivered by extraperitoneal cesarean section under continuous spinal anesthesia. The highest temperature after this was 101.4° and there were nine days of low-grade fever. She was discharged in good condition on the fourteenth postoperative day.

CASE 16.—(Pennsylvania Hospital.) A 23-year-old Negro, gravida i, para 0, at term, had been in labor with ruptured membranes for 59 hours. There was cephalopelvic disproportion and the head was unengaged. The uterus was tender and there was secondary uterine inertia. The fetal heart sounds were present. There was an odorous vaginal discharge and the patient looked quite ill. Temperature was 100.4° F., pulse 120. An extraperitoneal section under continuous spinal anesthesia was done and a 7 pound 8 ounce living male child delivered. There was a temperature of 103° F. postoperatively and a wound abscess developed which caused a low-grade fever for fourteen days. Discharged in good condition on the nineteenth postoperative day. Sixteen months later a second child was delivered by elective section.

CASE 17.—(Pennsylvania Hospital.) A 26-year-old Negro, gravida i, para 0, at term, had been in labor 31 hours and membranes had been ruptured for 44 hours. The uterus was tender and tense but fetal heart tones were still present. There was a foul discharge and the vertex was found to be high above the spines and overriding at the symphysis. There was 4 cm. dilatation of the cervix. The temperature was 102.4° F. and pulse 128. An extraperitoneal section under continuous spinal anesthesia was used to deliver a normal living 6 pound 3 ounce male infant. There was pus under pressure in the uterus. There was a temperature of 104° F. after this surgery and a mild incisional infection developed. Fever lasted for nine days. The patient was discharged on the eleventh postoperative day in good condition.

CASE 18.—(Pennsylvania Hospital.) A 28-year-old Negro, gravida iii, para 0, at term, came into the hospital after 72 hours of hard labor at home. The membranes had been ruptured 24 hours. Many unsterile vaginal examinations had been made in the home. The patient was tired and toxic and obviously infected. There was a foul discharge coming from

the vagina and the uterus was tender and tense. The head was not engaged and the diagonal conjugate measured 7.5 cm. An extraperitoneal section was done and a 6 pound 12 ounce living male infant delivered amid a gush of foul fluid. Upon the baby's head was an area which resembled a decubitus ulcer. The temperature at this time was 102.4° F. The fever lasted for six days but never went higher. There was a wound abscess. The patient was discharged on the twenty-second postoperative day. Three years later the patient, again at full-term pregnancy, allowed labor to start at home in spite of warnings. Upon entering hospital, a section was done and ruptured uterus found along the left broad ligament. The old incision was intact. A living child was delivered and a hysterectomy done. Recovery was complete.

### Comment

Such cases as these should not exist in this so-called enlightened day of obstetric achievement. This paper in no way upholds the management of these cases before they became infected or up until the time of delivery. It does, however, uphold the method of delivery by extraperitoneal cesarean section after the condition was recognized. While the maternal mortality in this series was zero, it is not intended to imply that such a record could go on indefinitely. There is an irreducible minimum mortality rate for every major surgical procedure.

How would those who decry the efficacy of extraperitoneal cesarean section have treated these cases?

Recently Settle and Wilson<sup>8</sup> have proposed that transperitoneal section with instillation of large amounts of sulfathiazole into the uterus, beneath the bladder flap, and in the peritoneal cavity is a method with which to treat potentially infected labor. There were no cases described which were as actually infected as the ones reported in this communication. A number of our cases upon whom extraperitoneal section was done had had penicillin and sulfonamide therapy for several days before becoming critically ill from infection. Another drawback to this method is the peritoneal irritation and the development of very tight adhesions which not only make subsequent surgery more difficult, but also give rise to the potential danger of intestinal obstruction and other alterations in intraabdominal physiology.

The only other methods are cesarean hysterectomy or embryotomy and, as has been pointed out, there are those who believe these methods should be used in exclusion of extraperitoneal cesarean section. In view of the evidence here presented, as well as that brought forward by others, it is hard to believe such a stand is any longer tenable.

It is occasionally good judgment to do a craniotomy on a dead baby if an easy delivery is made possible that way. The performance of a difficult embryotomy in a woman toxic and weakened by a long, fatiguing labor, as well as serious intrauterine infection, is another matter entirely, and it appears to the author to be outmoded and reprehensible even though the fetus be dead. Many

*Footnote:* Cases 12 to 18 were operated upon by Dr. C. C. Briscoe. Case 11 was furnished by Dr. J. Marsh Alesbury. Cases 1 to 10 were operated upon by the author, six at the Philadelphia General Hospital on the service of Dr. John C. Hirst, three were private cases done in consultation at the Episcopal Hospital, and one was done at the Jefferson Hospital on the service of Dr. Thaddeus L. Montgomery.



decades ago, difficult embryotomy was necessary because of the high mortality of cesarean section and the obstetricians of that day were undoubtedly much better technicians in its performance because of this. Today, very few indeed have developed this degree of competence.

Cesarean hysterectomy was originally devised to reduce the frightful mortality from infection associated with cesarean section. Today the indications for this procedure have widened and include ruptured uterus, intractable hemorrhage, Couvelaire uterus, uterine myomas, placenta accreta and, in some hands, as a method of sterilization. Moreover, textbooks still almost invariably mention intrauterine infection as an indication.

Reis and De Costa,<sup>9</sup> in their recent article, reviewed 731,690 deliveries reported from well-known clinics in the American literature since 1939. Six hundred fifty-six cesarean hysterectomies were done with a mortality of 5.2 per cent, which was approximately two and one-half times as great as the cesarean section mortality of 2.14 per cent. The individual series had mortalities for this procedure of from zero to over 22 per cent.

It is our feeling that cesarean hysterectomy in foully infected patients is dangerous. Although hysterectomy upon the gravid uterus is often easy to perform, it is a shocking procedure to the dangerously ill, violently infected patient. The peritoneal cavity is invaded and peritonitis is still liable to develop even though the uterus is removed. A condemning feature of this operation is the sacrifice of the uterus in primiparas, for it is usually the woman pregnant for the first time who has a prolonged infected labor. Of the eighteen patients mentioned here, fifteen were primigravidas.

Extraperitoneal cesarean section is not only much less traumatic and shocking than difficult embryotomy or hysterectomy, but also affords the fetus a chance of surviving and preserves the uterus. It is a simple incision of the uterus outside of the peritoneal cavity. It is well known that incision and drainage is one of the most efficacious procedures employed in surgery. The sulfonamides and antibiotics will not save a patient who needs drainage of pus under pressure. This has repeatedly been shown in general surgery, as well as in our series of profoundly infected cases of pregnancy, where extraperitoneal incision and drainage of the foully infected uterus have given excellent results. As has been shown, this operation is used at times when the fetus is known to be dead, and it appears that this traditional contraindication to cesarean section is no longer valid.

There have been numerous criticisms of extraperitoneal section technique, most of which lose significance after a little experience in doing the operation has been achieved. However, there is one which has not been definitely answered and we feel much as does Schumann,<sup>11</sup> who recently, at the American Congress of Obstetrics and Gynecology, remarked that he was "at a loss to explain why these patients with free pus in the uterine cavity yielding positive cultures of pyogenic bacteria do not go on and develop puerperal sepsis after extraperitoneal section."

That they do not is undoubtedly due to several factors, among which may be: the use of modern postoperative management; the prevention of peritoneal

soiling and the little trauma of the procedure; and the drainage of the tissues confluent with the parametrium which are reputed to be poorly resistant to infection and which are usually involved in the patient with puerperal fever.

The fact that women with the foulest of infections may be delivered safely by this method, all the while preserving the child-bearing organ, truly marks the newer technique of extraperitoneal cesarean section as a significant advance in modern obstetrics which should be recognized by all obstetricians until some simpler method, not yet known, appears to take its place.

### Summary

1. 38 per cent of all cesarean section deaths are due to infection and usually follow transperitoneal operations done upon cases which have violated certain important criteria.

2. There is disagreement over the best method for delivery of the infected patient who cannot be delivered vaginally of an intact infant. The difference of opinion lies between cesarean hysterectomy, embryotomy, extraperitoneal cesarean section and transperitoneal cesarean section with local administration of sulfonamides.

3. Infected cases treated by extraperitoneal cesarean section are reported without maternal mortality.

4. Transperitoneal cesarean section in infected cases is pointed out as dangerous even though advantage is taken of the modern antibiotics and chemotherapeutic agents.

5. Difficult embryotomy is pictured as being outmoded and reprehensible.

6. Cesarean hysterectomy is criticized as being a mutilating and dangerous procedure when used in primigravidas, even though severe intrauterine infection is present.

7. The modern technique of extraperitoneal cesarean section is the safest and simplest method of treating severely infected cases when vaginal delivery of an intact infant cannot be consummated.

*Note:* The author wishes to express his appreciation to Dr. Newlin Paxson, Dr. Clarence Briscoe, and Dr. J. Marsh Alesbury for allowing the inclusion of their cases in this paper.

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1814 SPRUCE STREET

### Discussion

DR. C. C. BRISCOE.—There has been a gratifying reduction in postcesarean sepsis recently; a result of such factors as earlier use of cesarean section, the prophylactic and active use of chemotherapeutic and antibiotic agents, the liberal replenishment of blood, and, when indicated, the exclusion of transperitoneal section and cesarean hysterectomy in favor of extraperitoneal abdominal delivery.

The failure of some clinics to adopt this procedure can be explained by their exclusive use of local anesthesia, an agent unsuited to extraperitoneal section. It would seem that some occasional desperate situations arise where minimal dose fractional spinal anesthesia might be used so that these babies, uteri, and lives could be saved.

These results should forever relegate to oblivion craniotomy on the living fetus. The reported 10 per cent fetal mortality is an eloquent plea for earlier section, but, even so, a ninety per cent fetal survival rate is considerably better than the absolute mortality obtained by craniotomy. Craniotomy on the dead fetus should be limited to cases of dystocia with the impacted head low in the pelvis, the hydrocephalic head low in the pelvis, and the aftercoming head. For inlet disproportion, extraperitoneal delivery is safer.

I fail to see why cesarean hysterectomy enjoys a good reputation as a means of treating infected women requiring abdominal delivery, for the reported mortality rate in all large series is about 10 per cent. It appears safer only by comparison with classical section under similar adverse conditions.

In both 1931 and 1941, cesarean hysterectomy accounted for ten per cent of the postcesarean septic deaths in Philadelphia, although less than two per cent of the sections performed were of this type. Most of these operations are done for uterine rupture, abruptio atony, or myomas, yet the mortality rate from sepsis alone was twenty per cent and 5.8 per cent, respectively, in these two years.

During the past fifteen years at the Lying-In Hospital, seven women had cesarean hysterectomy because of infection. Two died, another suffered severe generalized peritonitis for weeks, saved only by the grace of God and huge doses of penicillin. Of 315 cesarean hysterectomies, which I have collected, 85 were performed for infection and 15.2 per cent of these were fatal. This compares most unfavorably with the present mortality rate for extraperitoneal section of 1 per cent, and the prepenicillin rate of 3 per cent.

To know why these infected patients survive after extraperitoneal delivery, we must turn to the autopsy room. Frank, in his monograph, shows that most women who die of sepsis, following vaginal delivery, die from vascular extension of the endometrial infection, while only 23 per cent die of peritonitis. On the other hand, in 45 autopsies which I have studied, 80 per cent of the patients who died of sepsis following cesarean section succumbed from generalized peritonitis. Incidentally, generalized peritonitis was present in every patient who had been treated by hysterectomy. This means that the intact uterus usually confines its infection within the parametrium, unless there be vascular spread. On the other hand, transperitoneal section and cesarean hysterectomy permit gross intraperitoneal infective spill and subsequent leakage through suppurative suture lines. In the extraperitoneal section, original spill is avoided and subsequent suppuration is drained. From a growing experience with this operation, and these data I concur wholeheartedly with Dr. McCall's conclusions.

DR. J. ROBERT WILLSON.—I cannot quite agree with the previous discussant that the place of extraperitoneal section has been settled by this paper. It is, however, one of the very few papers that has presented any instructive material regarding the mortality rate in infected patients. The vast majority of reports have combined the sections done on infected patients, those done in potentially infected patients who might have been equally well handled by transperitoneal section, and those cases which were used simply for teaching material. If subsequent series such as Dr. McCall has presented show equally good results, it will certainly go a long way toward convincing some operators that it is a safe procedure. I do not think, however, we can discard completely the other methods of

delivering these patients. As has been pointed out, craniotomy is sometimes feasible if it can be done on the dead or damaged baby without increasing the maternal risk. It is preferable to making an incision in the uterus and asking the patient to have the rest of her babies by cesarean section. There is also a place for cesarean hysterectomy and I cannot agree that it is quite as formidable a procedure as has been suggested. The mortality rates presented for hysterectomy in the pregnant patient usually include the operations done for hemorrhage, ruptured uterus, etc., in addition to the true cesarean hysterectomy for infection, and consequently are distorted. We do not always know in which cases the uterus should be removed; it is difficult to tell. While these cases were without doubt badly infected. I would say that most of them were rather superficial infections of the uterus since the majority cleared up rapidly after delivery. The patient who has an infected uterus and myometritis with extensive abscess formation certainly is not going to do nearly as well, if the uterus is left, as these patients did. Many years ago, Baldwin reported a marked reduction in mortality in such patients by hysterectomy. The recent work of Falk in the treatment of septic abortions with widespread peritonitis by hysterectomy also suggests that this procedure is valuable, since the infections in each instance are comparable. I would hesitate to give up any one of the three methods of delivering these infected patients since it seems that no one procedure can be applied to every case.

DR. NEWLIN F. PAXSON.—I too have become enthusiastic concerning this operation. New processes have to be subjected to many analyses before they are part of a standard procedure. It seems to me we have gotten far enough along to realize that it should be part of the armamentarium of every large clinic. We teach at Hahnemann, in our ward cases, that all cases of labor needing cesarean section must have extraperitoneal cesarean and by that method we are training the junior staff obstetricians and residents. Our series is now up to some fifty cases plus and still no maternal deaths. We also teach that there is a place for craniotomy where the cervix is fully dilated. I am opposed to vaginal operation for delivery through an incompletely dilated cervix. When the cervix is dilated, or the baby is dead, or there is an aftercoming head, craniotomy is the better operation. We reserve cesarean hysterectomy for problems of uterine disease complicating pregnancy, fibroid, etc., but when we come to sepsis during labor we feel that extraperitoneal section has answered our needs more satisfactorily than any procedure so far.

DR. EDWARD A. SCHUMANN.—So far as I am aware, this is the first paper which describes the use of extraperitoneal cesarean section in a series of profoundly infected patients and one cannot avoid being deeply impressed by the fact that many of these patients would, in all probability, have been doomed to death by any form of intraperitoneal cesarean section. The postoperative course, even in these badly infected women, has been so smooth that one is impelled to the belief that, as soon as competency in performing this operation has become widespread, it will probably replace all other types of cesarean section even in the elective cases because, if the risk of intraperitoneal infection can be avoided by a technique not too involved, it follows that this precaution becomes almost automatic. With regard to hysterectomy following cesarean section, this operation has always been repugnant to me. It is a confession of abject defeat on the part of the physician in handling a complication of the reproductive function. Personally, I see no reason to perform hysterectomy following cesarean section except in a uterus obviously diseased beyond redemption. Multiple fibroids, profound infiltration with blood, extensive rupture, such conditions may warrant the removal of the organ but certainly not infection of a doubtful degree. Here the extraperitoneal cesarean section is the operation of choice. Cesarean section in the presence of a dead infant has been considered improper obstetrics but I feel very strongly that, in the event of a firmly impacted dead fetus, where embryotomy would involve the difficulties and traumatisms so often associated with this procedure, the extraperitoneal cesarean section is a far safer method of delivery. Difficult embryotomies are so uncommon that there are but few obstetricians who have developed the skill necessary to perform such an operation, particularly upon an exhausted and infected woman, without grave danger. Therefore, I feel that extraperitoneal section will solve many of these problems.



DR. THADDEUS L. MONTGOMERY.—Dr. McCall's paper is of particular value because it goes a long way in helping to establish the efficacy of the extraperitoneal type of cesarean section in the treatment of the infected patient who requires abdominal delivery. The cases which he has gathered from his own experience, and from the experience of several other operators in Philadelphia who have performed the majority of these operations, were truly infected patients and answer fully the criteria which Dr. Dieckmann has suggested. The number of cases is not large because there are not too many patients who fall into this category in modern obstetric practice, but the results are all the more impressive because they truly represent what can be accomplished in obtaining low morbidity, low mortality, and preservation of the childbearing function in these cases.

I have often wondered why the extraperitoneal operation gives so much better results in the potentially infected or actually infected patient than the transperitoneal low cesarean section, because it is difficult to believe that a thin layer of translucent peritoneal tissue will act as a barrier to infection entering the peritoneal cavity. Also, it frequently happens that this peritoneum is nicked or traumatized in the course of operation and has to be closed, and quite likely there are abrasions or areas which are not recognized and permit of some access of fluid and bacteria into the peritoneal cavity. My own opinion is that actually the peritoneal cavity is possibly more resistant to infection than is the connective tissue of the parametrium and that the important factor in the extraperitoneal operation is the establishment of a tract for thorough drainage of the extraperitoneal field following operation. This thorough drainage plus the use of antibiotics provides for the protection of the peritoneal cavity from infection, in addition of course to the avoidance of any gross spill into the peritoneal cavity at the time of operation.

While there is still a place for the procedure of cesarean section and hysterectomy in certain infected patients and, of course, in not a few patients with neoplasms complicating pregnancy and various hemorrhagic conditions, yet the extraperitoneal operation of cesarean section has been found to have great value and has lessened the number of instances in which hysterectomy is essential.

DR. McCALL (Closing).—The main purpose of the paper was to record as many cases as we had seen of truly infected patients. As to technique, I might mention in closing that in Dr. Paxson's and Dr. Briscoe's series, the supravescical technique of Waters was used exclusively. In my series, twenty-one were done by the latter technique and thirteen by the paravesical technique of Norton, where more blunt dissection is used. Both of these techniques are excellent, indeed, although the method of Norton has been used more often in the recent cases.

## A REVIEW OF 445 PREGNANCIES COMPLICATED BY FIBROMYOMAS

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ONE or more cases of fibromyomas and pregnancy are constantly present on the ward service at the Sloane Hospital. Since proper treatment continues to be the basis of discussion and dispute, it was considered of interest to review the records of recent years.

### Incidence

Over 60,000 admissions to this hospital covering the period from its inception to 1931 have been reviewed and previously reported.

The present report covers an additional 20,763 obstetric admissions during the years 1934 to 1945, inclusive. There were 392 cases with a total of 445 pregnancies with complicating fibromyomas—an incidence of 2.1 per cent. This incidence exceeds those quoted in the literature (Table II) and shows an increase over previous reports from this hospital (Table I). Better records and an increase in the number of Negro admissions may account for this. Of the present cases 261 (66 per cent) were Negroes.

TABLE I. INCIDENCE OF FIBROIDS AT SLOANE HOSPITAL

YEARS	AUTHOR	NO. OF CASES	NO. OF FIBROIDS	PER CENT
1886-1915	Craigin and Ryder	20,000	89	0.45
1916-1924	Pierson	30,836	250	0.8
1925-1931	Watson	11,675	157	1.3
1934-1945	Present Series	20,763	445	2.1

TABLE II. INCIDENCES QUOTED IN THE LITERATURE

AUTHOR	PER CENT
Mussey, R. D., and Hardwick, R. S.	1.9
Browne, F. J.	0.28
Kosmak, G. W.	0.34
Campbell, R. E.	0.43
Emge, L. A.	1.3
Eisaman, J. R.	0.3
Duckering, F. A.	1.4
Buckell, E. W. C.	0.79

### Classification as to Significance

The significance of the fibromyomas was graded one plus to four plus, based on a combination of size, number, location, symptoms, and the opinion of the clinicians in charge.

The data in Table III reveal that 58 per cent of the cases were of significance.

TABLE III. NUMBER OF CASES IN RELATION TO SIGNIFICANCE

SIGNIFICANCE	NUMBER
0	187
1 plus	135
2 plus	66
3 plus	27
4 plus	30
Total "significant" cases	258

### Age

The average age was 32 years. As shown in Table IV, about 75 per cent were over 30 years. This age distribution is in accord with the age incidence of fibromyomas in general. It is noted that the patients, aged 30 years and over, make up 75 per cent of the over-all groups as well as the individual groups subdivided as to significance. Age is not related to the degree of significance of the fibromyomas.

TABLE IV. AGE AS RELATED TO SIGNIFICANCE AND NUMBER OF PREGNANCIES IN DIFFERENT AGE GROUPS

AGE	SIGNIFICANCE					TOTAL	PER CENT
	0	1 PLUS	2 PLUS	3 PLUS	4 PLUS		
Less than 20	3	1	0	0	0	4	0.9
20-29	46	31	18	6	8	109	24.5
30-39	128	91	41	17	19	296	66.5
40-49	10	12	7	4	3	36	8.1
Total	187	135	66	27	30	445	

### Parity and Gravidity

Two hundred twenty-seven (51 per cent) of the pregnancies occurred in primigravidas; 180 (40.5 per cent) had had one or two term pregnancies previously; the remaining 8.5 per cent had had more than two previous term pregnancies.

The data in Table V shows that parity and gravidity decreased inversely to the significance. However, in the cases of 0 to 3 plus significance, approximately 50 per cent had had a previous term pregnancy. The 4 plus group was marked by having 80 per cent primigravidas with only 13 per cent having had a previous term pregnancy.

TABLE V. PARITY AND GRAVIDITY AS RELATED TO SIGNIFICANCE

SIGNIFICANCE	P0	P1	P2	P3	P4	P5	P6	P7
0	84	56	23	12	7	1	3	1
1 plus	69	35	23	5	2	1	0	0
2 plus	34	21	7	2	1	1	0	0
3 plus	14	6	5	1	1	0	0	0
4 plus	26	4	0	0	0	0	0	0
Total	227	122	58	20	11	3	3	1

SIGNIFICANCE	G1	G2	G3	G4	G5	G6	G7	G8	G9	G10	G11	G12
0	70	57	36	13	1	3	4	1	0	1	0	1
1 plus	51	31	20	19	7	4	3	0	0	0	0	0
2 plus	27	16	9	9	0	3	1	1	0	0	0	0
3 plus	10	5	7	2	2	1	0	0	0	0	0	0
4 plus	24	5	0	1	0	0	0	0	0	0	0	0
Total	182	114	72	44	10	11	8	2	0	1	0	1

Eighty-five (21 per cent) of the patients had a total of 145 previous abortions. Six had a total of 13 induced abortions without any history of sepsis following. However, it is difficult to obtain an accurate history on the latter type of case.

The most that one can deduce from the above figures is that relative infertility exists in patients with fibromyomas.

### Labor Time

The duration of labor was not increased in this series, nor was there any correlation between duration of labor and the significance of the fibroids. This is in contrast to a generally held opinion that fibromyomas increase labor time.

Table VI demonstrates the latter statement. Primiparous labors averaged 15 hours, 42 minutes and multiparous labors ten hours, six minutes. Of 307 labors, 35 (11 per cent) were cases of prolonged labor (greater than 30 hours) and 17 (5 per cent) were cases of precipitate labor (less than 3 hours). Campbell reported 26 per cent prolonged labors and 49 per cent of his cases with shorter labors than normal.

TABLE VI. DURATION OF LABOR IN RELATION TO SIGNIFICANCE AND PARITY

SIGNIFICANCE	PRIMIPAROUS LABORS		MULTIPAROUS LABORS	
	NO. CASES	AVERAGE TIME (HOURS AND MINUTES)	NO. CASES	AVERAGE TIME (HOURS AND MINUTES)
0	56	16:12	74	11:51
1-2 plus	77	15:45	76	9:20
3-4 plus	15	12:25	9	15:22
Average time per group		15:42		10:06

### Size of Fibromyomas

As seen in Table VII, increased size of the fibroids was correlated with increased significance. Thus, of 187 cases of no significance, only 3 per cent were 6 cm. or more in diameter. Seven per cent of the 1 plus group, 51 per cent of the 2 plus, 60 per cent of the 3 plus and all of the 4 plus cases exceeded 6 cm. in diameter. In the groups of low significance, size is not a prime factor.

TABLE VII. THE SIZE OF THE FIBROIDS RELATED TO SIGNIFICANCE

SIGNIFICANCE	SIZE IN CENTIMETERS			
	2-2.9	3-5.9	6-9.9	GREATER THAN 10
0	106	76	5	0
1 plus	39	84	11	1
2 plus	4	28	32	2
3 plus	3	8	14	2
4 plus	0	0	20	10

In 53 cases, the fibroids increased in size during the antepartum course. A decrease in size post partum occurred in 104 cases. The fibroids that enlarged antepartum did not necessarily decrease in size after delivery.

There were 53 successive pregnancies recorded.

In Table VIII the course of fibroids as regards size is demonstrated in succeeding pregnancies. Emge contended that fibroid enlargement during pregnancy is temporary and that in subsequent pregnancies, fibromyomas occasionally enlarge or enlarge to a lesser degree. This series only partially agrees with Emge's conclusions.



During the antepartum course, 72 per cent of the fibroids were first noted; 19 per cent were noted the first time at term and 9 per cent first diagnosed post partum. The greater the size of the fibroids, the earlier the time of detection.

TABLE VIII. COURSE OF FIBROIDS IN SUCCESSIVE PREGNANCIES

SUBSEQUENT PREGNANCIES	NO. OF CASES
No change in size	32
Increased size	10
Decreased size	11
Total	53

### Degeneration of Fibroids

Only one of four fibromyomas evidenced degeneration. Degeneration was variable in successive pregnancies. Of the cases that degenerated in the first pregnancy, 6 per cent did not degenerate subsequently, whereas 10 per cent that did not evidence degeneration in the first pregnancy did degenerate in later ones.

### Antepartum Course

Table IX reviews the antepartum course. One hundred and twenty-five (28 per cent) had pain of varying degrees. In the 53 successive pregnancies, 15 per cent had pain in first pregnancies and none subsequently, whereas 7.5 per cent had no pain in first pregnancies, but did have pain in following ones.

TABLE IX. COMPLICATIONS OF ANTEPARTUM COURSE

SIGNS, SYMPTOMS, AND PATHOLOGY	NO. OF CASES
Pain	125
Bleeding	50
Fever due to fibroids	4
Varices (vulval and extremities)	8
Urinary obstruction	2
Respiratory and cardiac distress	2
Toxemia	46
Hypertensive vascular disease	24
Torsion of fibroids	0
Infection of fibroids	0
Early abortions	8
Late abortions	14

Sedimentation rates were not recorded constantly enough to be evaluated.

The abortion rate of the 445 cases herein reported was 5 per cent, a low rate compared to the usual estimate of the "normal" rate of abortion which is about 20 per cent.

The toxemia and hypertension incidence was 10 and 5 per cent, respectively—the same as the generally prevailing rate.

No fibroids became infected ante partum but three did post partum.

Table X demonstrates that hemoglobin values are unaffected by the fibromyomas. The higher hemoglobin values in the more severe cases are not significant.

TABLE X. AVERAGED HEMOGLOBIN VALUES ANTE PARTUM

SIGNIFICANCE	HGB. PER CENT
0	77.5
1-2 plus	79.5
3-4 plus	85.0

Ten per cent of the cases were operated upon ante partum.

The operations and the indications are listed in Table XI. Of the three myomectomies, only one continued to term to be delivered by cesarean section. One of the laparotomies for ovarian cyst proved to be an error in diagnosis, a fibroid was present.

TABLE XI. OPERATIONS WITH INDICATIONS ANTE PARTUM

OPERATION	NO.	INDICATION	NO.
Hysterectomy	18	Fibroids	6
		Degenerating fibroids	2
		Fibroids and hypertensive vascular disease	5
		Fibroids and pyelonephritis	1
		Fibroids and toxemia	1
		Fibroids and exophthalmic goiter	1
		Fibroids and anxiety neurosis	1
		Fibroids and undiagnosed pulmonary disease	1
Dilatation and curettage	16	Incomplete abortion	12
		Therapeutic abortion	4
Myomectomy	3	Fibroids	3
Myomectomy and hysterotomy and sterilization	4	Fibroids and hypertensive cardiovascular disease	3
		Fibroids and Boeck's sarcoid	1
Myomectomy and hysterotomy	1	Fibroids and rheumatic heart disease	1
Appendectomy	1	Acute appendicitis	1
Laparotomy for ovarian cysts	2	Ovarian cyst	2
Total	45		

### Labor

The data in Table XII show the presentation present at term or during labor. The malpresentation incidence was two to three times the stated average incidence.

TABLE XII. PRESENTATION AT TERM AND DURING LABOR

PRESENTATION	NUMBER
Vertex	355
Breech	28
Twins	6
Transverse	4
Face	3

TABLE XIII. COMPLICATIONS OF LABOR

COMPLICATIONS	NUMBER	PER CENT
Premature rupture of membranes	106	21.0
Premature delivery	14	3.1
Uterine inertia	32	7.2
Dry labor	0	0
Mechanical obstruction	6	1.3
Prolapse of cord	6	1.3
Retained placenta	8	1.8
Prolonged labor (more than 30 hours)	35	11.0
Precipitate labor (less than 3 hours)	17	5.0
Postpartum Hemorrhage	19	4.3

A list of the complications of labor is presented in Table XIII. The incidence of premature delivery is not excessive. Prolapse of the cord occurred with average incidence; in four of the cases the prolapse was attributed to malpresentation. Postpartum hemorrhage occurred with less than the usual incidence, whereas retained placenta occurred twice as often.

### Delivery

Four hundred two cases, 90 per cent of the recorded pregnancies, came to delivery. Of these, 247 (61 per cent) delivered spontaneously.

One hundred fifty-five (39 per cent) were operative deliveries. Of the latter, 95 were cesarean sections.

The section rate for term pregnancies was 21.3 per cent. If correction is made to include only those cases where fibromyomas made up the whole or part of the indication, the rate was 12.8 per cent. See Table XIV.

TABLE XIV. INDICATION FOR CESAREAN SECTION

INDICATION	NO. CASES	NO. CASES WITH MULTIPLE INDICATIONS
Dystocia due to myoma	26	12
Painful or degenerating fibroids	12	5
Elderly primiparas with fibroids	20	15
Disproportion	39	21
Elderly primiparas with sterility	4	3
Elderly primiparas with poor labor	4	3
Previous section or myomectomy	18	9
Elderly primiparas with breech	2	2
Eclampsia	0	0
Severe pre-eclampsia	3	2
Premature separation of placenta	2	0
Placenta previa	3	0
Chronic nephritis	0	0

Of the 95 sections, 26.3 per cent were classical, 28.2 per cent low flap, 45.3 per cent cesarean plus supravaginal hysterectomy and 1.1 per cent Latzko extra-peritoneal section. Table XV further analyzes the sections.

Of the twenty-four patients who had myomectomies, eleven subsequently became pregnant again, ten delivering by repeat sections and one delivering spontaneously.

TABLE XV. CESAREAN SECTIONS

TYPE OPERATION	NUMBER	PER CENT
Classical	5	5.26
Classical and myomectomy	14	14.73
Classical and myomectomy and sterilization	2	2.10
Classical and sterilization	4	4.20
Low flap	15	15.77
Low flap and myomectomy	10	10.52
Low flap and sterilization	2	2.10
Cesarean with supravaginal hysterectomy	43	45.26
Latzko extraperitoneal	1	1.05

Table XVI reviews the operative procedures used in the course of delivery.

The antepartum and term operative procedures totaled 200 or 44.9 per cent of the recorded pregnancies. Compared to the operative incidences of 48 per cent and 46.5 per cent as reported by Watson and Pierson at Sloane, there has been no significant diminution through the years.

TABLE XVI. OPERATIONS AT TERM

OPERATION	NUMBER	PER CENT
Cesarean section	95	61.3
Low forceps	20	12.9
Midforceps	9	5.8
Assisted breech	25	16.1
Version-breech extraction	2	0.65
Dührssen's incisions	1	0.65
Manual removal of placenta	1	1.23
Craniotomy	2	1.23
Total	155	

The indications for cesarean section are listed in Table XIV. It is noted that many of the indications were multiple, leaving only 14 with dystocia due to myoma, 7 with degenerating fibroids, and 5 elderly primiparas with fibroids as the sole indications for section. Another 35 had sections primarily for reasons exclusive of fibroids.

### Morbidity

Of the 445 cases, 118 (26 per cent) had a postpartum or postoperative morbid course. This morbidity rate is three times the eleven-year average incidence at Sloane.

A review of Table XVII shows that the highest operative morbidity is associated with cesarean section, the lowest with cesarean section plus myomectomy. The morbidity for cesarean and supravaginal hysterectomy, though far below that of cesarean sections, is above that for cesarean and myomectomy. Huber and Hesseltine claimed that cesarean plus supravaginal hysterectomy yielded the lowest morbidity. This series does not support the latter contention. There would appear to be no contraindication to doing myomectomy as far as morbidity is concerned.

TABLE XVII. MORBIDITY RATE FOR DIFFERENT MODES OF DELIVERY

MODE OF DELIVERY	NO. CASES	PER CENT MORBIDITY
Spontaneous	247	14.7
Forcep and breech	54	48.8
Cesarean section	20	85.0
Cesarean section and myomectomy	28	42.1
Cesarean section and supravaginal hysterectomy	43	48.8

About 10 per cent of the total cases exhibited subinvolution post partum.

The mortality rate was 0.6 per cent. In Cases A and B in Table XVIII, fibromyomas were important causative factors.

TABLE XVIII. SUMMARY OF FATALITIES

Case A.—Spontaneous delivery; subsequent intestinal obstruction due to adhesions between a fibroid and sigmoid.
Case B.—Prolonged labor, midforceps, peritonitis secondary to degenerating fibroid.
Case C.—Therapeutic abortion and sterilization for hypertension and fibromyomas; postoperative intestinal obstruction.

### Fetal Mortality

As indicated in Table XIX, the over-all fetal mortality is high. Early, late, and therapeutic abortions are the prime contributors to the high rate. If, among the neonatal deaths, the three so-called previable births are excluded, a corrected fetal mortality rate of 36 per thousand is obtained, which is comparable to the corrected fetal mortality rate for all pregnancies at this hospital.

The absence of fetal mortality following cesarean section is noteworthy.



### Hospital Days

The average stay in the hospital was 14.5 days. Thus, fibromyomas are also an important economic and administrative factor.

TABLE XIX. FETAL DEATHS AND ACCOMPANYING METHOD AND TIME OF DELIVERY

METHOD AND TIME OF DELIVERY	NUMBER
Early, late, and therapeutic abortions	43
Miscarriage (20 to 28 weeks)	8
Stillborn	7
Neonatal	
24 weeks, spontaneous	1
20 weeks, spontaneous	1
18 weeks, spontaneous	1
Term, spontaneous	2
Term, assisted breech	1
Term, spontaneous breech	1
Term, midforceps	1
Cranioclast	1
Uncorrected fetal mortality rate	150/M
Corrected fetal mortality rate	36/M

### Comment and Summary

A review of 20,763 obstetric admissions is presented. Of these, 445 had complicating fibromyomas, an incidence of 2.1 per cent. Two hundred fifty-eight were rated as significant. Significance was graded from one plus to four plus.

The average age of the patients was 32 years. Seventy-five per cent of the patients were over 30 years of age. Age and degree of significance did not correlate. Parity and gravidity decreased as the significance increased. This was most marked in the cases of four plus significance. Fifty-one per cent of the patients were primigravidas. Relative infertility and fibroids seemed to go hand in hand.

Labor time was not prolonged by fibroids. Primiparas averaged 15 hours, forty-two minutes and multiparas ten hours, six minutes.

Fibroid enlargement in pregnancy is frequently but not always temporary. Only one of four fibroids evidenced degeneration. Degeneration was variable in multiple pregnancies. Six per cent of the cases that degenerated in the first pregnancy did not degenerate subsequently. Ten per cent that did not evidence degeneration in the first pregnancy did degenerate subsequently.

During the antepartum course, 28 per cent complained of pain. Of the successive pregnancies, 15 per cent had pain in the first pregnancy, none in subsequent pregnancies. Four, or 7.5 per cent, had no pain in the first pregnancy but pain in subsequent ones. Eleven per cent had varying degrees of bleeding. Hemoglobin levels were unaffected by the fibromyomas.

Five per cent of the cases aborted, a very low abortion rate. Toxemia and hypertensive disease showed an incidence of 10 and 5 per cent, respectively, the same as the generally prevailing rates.

Forty-four (10 per cent) of the patients were operated upon in antepartum courses. Of these, 40.9 per cent had hysterectomies and 18.1 myomectomies. Three of the latter had myomectomies only and, of these three, only one continued to term and was terminated by section.

Malpresentations occurred with two to three times the usual incidence. There were 14 premature labors, an incidence of 3.1 per cent—about average.

Postpartum hemorrhage in 19 cases showed an incidence of 4.3 per cent. This is less than the usual incidence for all pregnancies. Retained placenta occurred eight times, an incidence of 1.8 per cent—twice the usual incidence. Ninety per cent of the cases came to delivery; of these, 247 delivered spontaneously and 155 were operative deliveries. Of the latter, 95 were cesarean sections, 29 were forceps deliveries. Nine, or 31 per cent, of the forceps were of the midforceps variety. The total operative incidence equalled 44.9 per cent—about the same as previously reported at this hospital.

Of 24 patients on whom myomectomies were performed, 11 subsequently became pregnant; 10 delivered by section, 1 spontaneously.

The cesarean section rate was 21.3 per cent. Corrected for fibroids as part or the whole of the indication, the rate was 12.8 per cent.

The morbidity rate was 26 per cent. This is three times the usual rate at Sloane. The morbidity rate for cesarean plus myomectomy was lower than that for cesarean hysterectomy. On the basis of morbidity there appeared to be no contraindications to cesarean plus myomectomy. Morbidity remains a prominent feature of fibromyomas and pregnancy.

Three patients died, a mortality rate of 0.67 per cent. This is a significant rate but lower than previously reported at Sloane.

If therapeutic abortions and spontaneous abortions are included, the fetal mortality is 150 per thousand. Corrected for viable fetuses, the rate becomes 36 per thousand—comparable to our over-all fetal mortality rate.

The rate of postpartum subinvolution was 10.3 per cent. The average hospital stay was 14½ days. Thus, fibroids become economically and administratively important.

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## ANEMIA OF PREGNANCY TREATED WITH MOLYBDENUM-IRON COMPLEX\*

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REPORTS from our clinic in 1936 indicated that 11.5 per cent of our pregnant patients were anemic according to our standards for pregnancy; but if the standards for nonpregnant patients are used, then 63 per cent must be classed as anemic. Comparable figures for the 1947 group are 4.6 per cent with anemia of pregnancy and 39 per cent, using nonpregnant standards. The methods used are essentially the same, and we have studies in progress to determine the reason for the decrease in the number of anemic patients. In 1936, we stated that the control anemic patients showed as great an increase in hemoglobin formation during pregnancy as the anemic patients who received adequate amounts of ferrous or ferric salts. Our impression at that time was that iron salts were of comparatively little value in the treatment of anemia of pregnancy.

Talso and Dieckmann, in a recent report of 250 cases of pregnant patients with anemia, concluded that the administration of various iron preparations as well as various vitamin concentrates did not cause a significant increase in the rate of hemoglobin formation.

Healy, in 1946, stated that the administration of a molybdenum-iron complex seemed to be more efficacious in the treatment of nonpregnant anemia than iron alone.

Neary, also, in 1946, reported that molybdenum-iron complex resulted in an average gain in hemoglobin of 4.6 Gm. in 6.2 weeks as compared with 2.1 Gm. in 6.9 weeks for ferrous sulphate in pregnant anemic patients. There were only eleven patients in each group. He reported no failures with the special iron salt.

Initial and periodic hemoglobin determinations are very important parts of prenatal and postpartum care. The usual methods for determining hemoglobin—either with the visual or photoelectric colorimeter—require very small amounts of blood, 0.02 ml. and dilutions of 100 to 400 times. Thus the combined error of the pipette and chamber as well as the technician may be 7 per cent to 15 per cent. The hemoglobin concentration may fluctuate as much as 15 per cent (accurate method) and the hematocrit 7 per cent during a twelve-hour period. The hematocrit and erythrocyte count are methods for determining the number of red blood cells per unit of blood. The hematocrit has a closer correlation with the hemoglobin concentration than the red-cell count because the error in the former is approximately 2 per cent, while the minimum error in the red-cell count is over 8 per cent. For over ten years we have been using the hematocrit determination on heparinized blood as a screening method.

\*The molybdenum-iron complex (Mol-iron) was supplied by the White Laboratories, Inc., Newark, N. J.

Comparisons of the determined versus the calculated hemoglobin concentration indicated that the mean error in the clinic laboratory was 0.6 Gm. and in the chemistry laboratory 0.28 Gm. The normal standard for women is hemoglobin, 14.3 Gm., hematocrit, 43 per cent (heparin), and erythrocyte, 5 million.

Any patient who is less than twelve weeks pregnant or more than six weeks post partum whose hematocrit is less than 37 volumes per cent (12.0 Gm. per cent) is referred to the antepartum anemia clinic. Between twelve weeks and thirty-six weeks' gestation, the lower limit of the hematocrit is 30 (10 Gm. per cent), and between thirty-six weeks and term the lower limit is 32 volumes per cent (10.5 Gm. per cent). The procedure in the anemia clinic is to obtain additional history and special examinations as to possible causes for the anemia. A diet history is obtained in some instances. The hemoglobin, hematocrit, red-cell count, leucocyte count and differential determinations are made. The various indices, mean corpuscular hemoglobin concentration and individual cell volume, etc., are determined and the anemia classified. All cases complicated by blood loss, toxemia, and infection were excluded in this study.

After a preliminary observation period of two to six weeks during which the determinations were repeated, therapy was begun. A capsule containing 3.0 mg. of molybdenum sesquioxide (approximately 2.5 mg. molybdenum) and 195 mg. of ferrous sulphate (approximately 40 mg. iron) was given to these patients (2 capsules three times a day, after meals). They contained no significant amounts of copper. Complete blood studies had been made and the hemoglobin, hematocrit, and red blood count were repeated every two weeks.

Data given in Table I show the percentage of patients with hemoglobin concentrations for our 1936 (3 yrs. 8 mos.) report and for a recent group (1 year) of patients from our clinic. It is obvious that there is a marked decrease in the number of anemic patients both in the clinic and private patient groups. Patients are not routinely given iron in any form. The only vitamin preparation is one containing A and D. The income of our patients is much higher today than it was in the period from 1933 to 1936. Considerable pressure is put upon each patient to see the dietitian but that does not mean that every patient does so nor does it mean that every patient follows the outlined diet.

TABLE I. FREQUENCY DISTRIBUTION OF HEMOGLOBIN CONCENTRATIONS IN PREGNANT PATIENTS

HEMOGLOBIN GM. PER 100 ML.	STAFF PATIENTS PER CENT		PRIVATE PATIENTS PER CENT	
	1936	1948	1936	1948
5- 5.9	0.06	0.03	0	0
6- 6.9	0.4	0.03	0	0
7- 7.9	1.0	0.28	0	0.08
8- 8.9	3.0	1.1	1.2	0.71
9- 9.9	7.0	3.2	5.9	2.8
Per cent of patients less than 10 gm. per cent	11.5	4.6	7.1	3.6
10-10.9	20.0	10.7	19.0	10.7
11-11.9	32.0	23.9	29.0	14.0
Per cent of patients less than 12 gm. per cent	63.5	39.2	55.1	28.3
12-12.9	23.0	30.9	29.0	35.3
13-13.9	10.0	25.0	13.0	32.0
14-14.9	3.0	4.3	1.7	3.1
15-15.9	0.6	0.63	0.7	1.0
16-16.9	0.06	0.03	0	0
17+	0	0	0	0.24
Total number of cases	7,835	3,520	170	1,274



There were 49 patients in the treated group and 39 in the control group. Eight per cent of the treated group were normocytic, 10 per cent had a macrocytic anemia, and 81 per cent were microcytic. The control group were essentially the same. The nine patients comprising the normocytic and macrocytic groups all showed increases in hemoglobin, patients with the normocytic anemia showing the maximum increase. Two per cent of the patients with microcytic anemia showed a decrease even though they took adequate amounts of the iron complex. The erythrocytes of 28 per cent of the patients with microcytic anemia were hypochromic, 66 per cent were normochromic and 6 per cent were hyperchromic.

Heath, Murphy, and Fullerton have each stated that, if the hemoglobin is less than 8 Gm. per 100 ml., the hemoglobin concentration, if adequate iron therapy is administered, should increase 1 per cent or 0.16 Gm. per day. The maximum increase is reached between the second and fourth weeks. Below 8 Gm. and above 12 Gm. per cent in the nonpregnant patient the rate of increase is much less.

Forty-five patients gained an average of 2.11 Gm. hemoglobin before delivery; the minimum was 0.6 and the maximum was 5.5 Gm. Four patients showed no significant change. One could not take the medicine and another had a severe pyelitis which could not be treated (the patient was sensitive to all sulfonamide drugs and the causative bacillus had become resistant to streptomycin). We could not determine any cause for the persistent anemia in the other two patients, except the pregnancy. All four patients had low normal hemoglobin concentrations when examined two or more months after delivery. We do not believe that the anemia of pregnancy is due to the fetal demands for iron.

TABLE II. CHANGES IN HEMOGLOBIN CONCENTRATION IN THE TREATED GROUP

HEMOGLOBIN GM. PER 100 ML.	DURATION OF TREATMENT			
	2 WEEKS	3 TO 4 WEEKS	5 TO 6 WEEKS	6 WEEKS +
Decrease	2	1		
No change	0	1		
Increases				
0.1- .49	6	0		
0.5- .99	8	7	1	1
1.0-1.49	9	5	5	0
1.5-1.99	4	5	2	1
2.0-2.49	2	7	5	1
2.5-2.99	1	2	2	3
3.0-3.49		1	4	4
3.5-3.99			2	1
4.0+			2	
Mean increase-Gm.	1.1	1.73	2.36	2.7
Number of Patients	32	29	23	11

Table II illustrates the periods of treatment as well as the increases of hemoglobin for each period. Many of the patients appear in more than one period. Some patients showed the optimum increases for the period studied. The mean increases at two and four weeks, however, do not amount to 1 per cent per day but are approximately 0.08 Gm. per day. The increase at six weeks, however, is not quite as great as one would expect, but it must be remembered that by this time many of the pregnant patients had hemoglobin concentrations that were within the normal range for pregnancy and obviously would not show the expected increase. The most outstanding finding is that after two weeks only two out of 32 patients showed a further decrease and at four weeks only one showed a decrease and one no change. We have never had



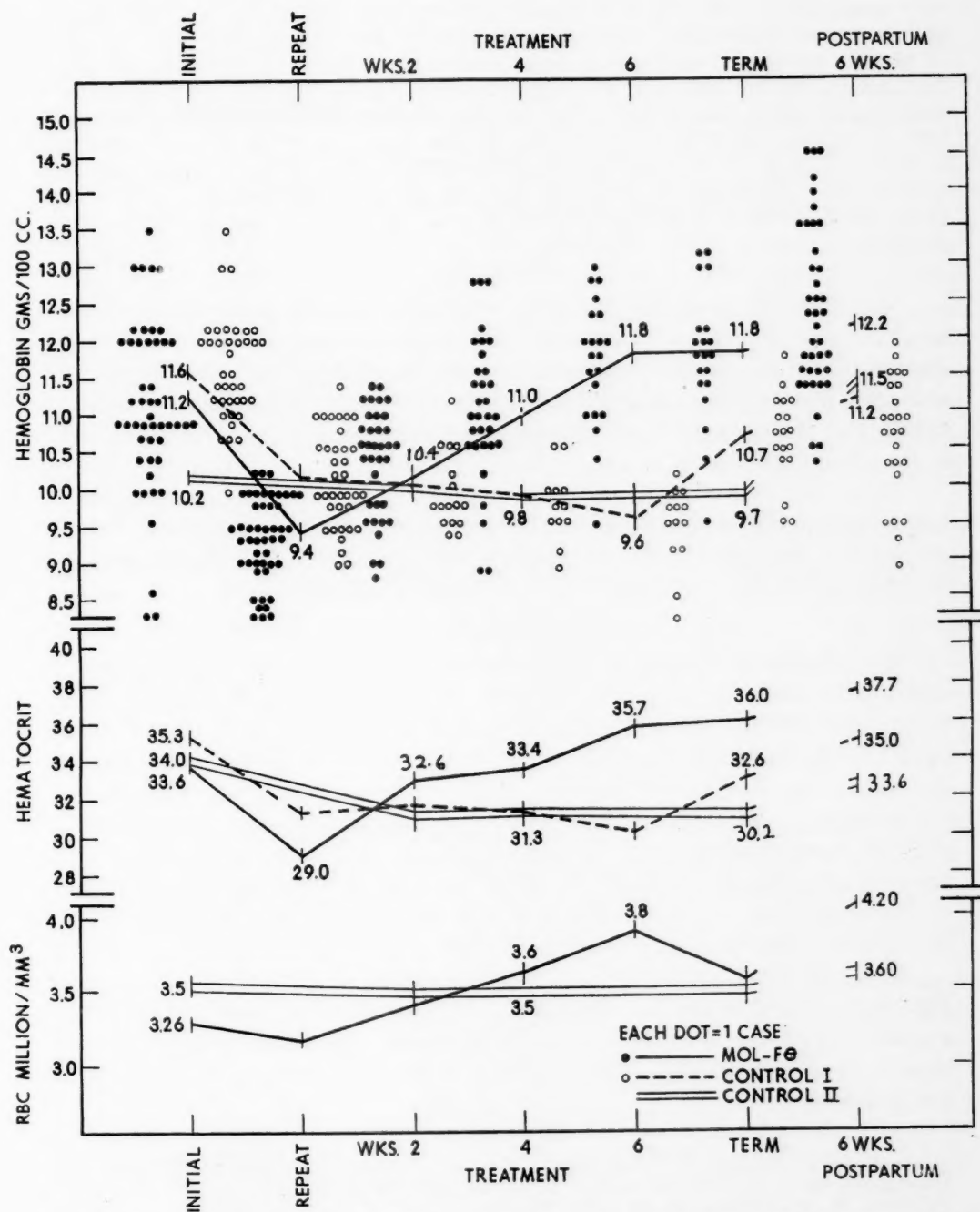


Fig. 1.—Therapy was started after the repeat determination in the treated group. Solid dot indicates treated case and circle is a control. Control curve I is untreated anemic patients followed in present study. Control curve II is taken from Talso-Dieckmann study based on patients studied between 1936 and 1945.

Table IV contains data from two pregnancies in R.D., number 349096, a 24-year-old private patient of the senior author. This woman is intelligent and very cooperative. Extensive studies of her diet and protein balance were made in her second pregnancy. The average protein intake was 78.4 Gm. per day (1.61 Gm. per kilo), and the average food iron intake was 10.9 Mg. per day. The months of the year and the hemoglobin levels for the two pregnancies are exactly the same. In a six-week period in the 1946 pregnancy, while taking 1 Gm. of ferrous sulphate daily, the hematocrit increased from 31 to 32 and the hemoglobin from 9.8 to 10.5. In the 1948 pregnancy in a five-week period, the hematocrit increased from 31 to 36 and the hemoglobin from 9.8 to 11.6 and three weeks later at term the hematocrit was 41 and the hemoglobin 13.2 Gm. per cent.

### Discussion

The increases in hemoglobin were so dramatic and so rapid that we postulated a possible decrease in plasma volume. A few studies, however, have indicated that there was no decrease in the plasma volume and the consistent and sustained increase in hemoglobin extending into months after delivery indicate even better than blood volume determinations that there was an actual increase in the amount of hemoglobin.

There were no alterations in the patients' diets to which the increases in hemoglobin might be attributed. So far as we can tell the control and treated groups are identical. Only one patient stated that she had to decrease the amount because of the gastrointestinal discomfort.

### Summary

The hematocrit determination is an easy, rapid, and accurate method of determining which patients have anemia. It is more accurate than the hemoglobin concentration as it is usually determined. Pregnant patients should have a hematocrit determination every three months, one at or near term, and one also at six weeks post partum. A hemoglobin which is less than 12 Gm. (hematocrit 37 per cent) in the first twelve weeks or which is not 12 Gm. or more six weeks post partum is indicative of anemia. From the twelfth to the thirty-sixth week the lower limit of the hemoglobin in pregnancy is 10 Gm. (hematocrit 30 per cent) per 100 ml. The lower limit from 36 weeks to term is 10.5 Gm. (hematocrit 32 per cent) per cent.

A molybdenum-iron complex has been found to be very effective in causing significant increases in the hemoglobin concentration of most patients with anemia of pregnancy within a three-week period. If the hemoglobin does not show a significant increase in this period of time, further hematologic studies are indicated.

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## THE TIME OF RECURRENCE OF ENDOMETRIAL CARCINOMA

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**M**ALIGNANT tumors differ from one another in their characteristic rate of growth. Some, such as basal-cell carcinomas of the skin, are typically slow in their development and spread; while others, like malignant melanomas, are notoriously rapid in their dissemination through the body and their usually fatal termination. Tumors of the uterus occupy an intermediate position in this respect. The time of recurrence of a series of epidermoid carcinomas of the cervix after radiation therapy has been reported in another study. The present paper presents data concerning the rate of growth of adenocarcinoma of the endometrium.

Information bearing on this problem has been obtained from a study of three groups of cases. The first group comprises patients who presented clinical evidence of tumor recurrence at varying intervals following treatment for carcinoma of the endometrium. Group 2 consists of patients in whom corpus cancer was recognized after the administration of intrauterine radium for presumably benign lesions but whose original curettings on restudy showed carcinoma to have been present. Group 3 includes patients in whom the diagnosis of endometrial carcinoma was missed at the initial curettage and who received no other treatment until the later discovery of the tumor.

**GROUP 1.**—The gynecologic files of the Roosevelt Hospital contain records of 42 treated cases of carcinoma of the endometrium in which the time of recurrence of the tumor was noted in the history. Forty-one of the recurrences occurred within 5 years of treatment. These cases are summarized in Tables I to IV. The unincorporated case is reported in detail because of its unusual interest.

TABLE I. INTERVAL BETWEEN TREATMENT AND RECURRENCE OF CARCINOMA OF ENDOMETRIUM

INTERVAL (MONTHS)	CASES	PER CENT
0-6	8	20
7-12	12	29
13-24	11	27
25-36	5	12
37-48	3	7
49-60	2	5
Total	41	100
Average interval		18.6 months

The distribution of the cases according to time of recurrence is presented in Table I. Practically half (49 per cent) of the recurrences were noted within the first year, and three-fourths (76 per cent) within the first two years. In a similar study of cervical cancer, 57 per cent and 84 per cent of the recurrences

were recorded during these respective critical periods. The fact that 41 out of 42 recurrent endometrial cancers were observed within five years of treatment confirms the practical safety of considering as probably cured patients who survive this period without evidence of recurrence. The average interval of recurrence in the 41 cases was 18.6 months, as compared with 14.5 months for patients with cervical cancer.

The type of treatment which was received by these uncured patients is shown in Table II, with the average recurrence interval for each type of treatment. With the exception of one case in which subtotal hysterectomy was performed, hysterectomy signifies removal of the entire uterus with both tubes and ovaries. The average dose of intrauterine radium, in the cases for which it was used, was 3,344 mg. hr. X-ray therapy, when employed, was usually given as a course of 16 to 20 treatments of 300 r. each through 4 pelvic ports, with the 200 kv. machine and protective filters of copper and aluminum. Although only six patients were treated with preoperative radium followed by hysterectomy, it is interesting that their average time of recurrence was only 12 months, as compared with 24 months in a larger group of patients who were treated by hysterectomy alone. This comparison indicates no advantage for preoperative radium, a conclusion which was also reached by another approach in a recent study of all the surgically treated cases of corpus cancer at the Roosevelt Hospital.

TABLE II. AVERAGE RECURRENCE INTERVAL OF ENDOMETRIAL CARCINOMA ACCORDING TO TYPE OF TREATMENT

TREATMENT	CASES	PER CENT	INTERVAL (MONTHS)
Hysterectomy	17	41	24
Radium	11	27	18
Radium and hysterectomy	6	15	12
Radium and X-ray	4	10	11
Hysterectomy and X-ray	2	5	11
Radium, hysterectomy and X-ray	1	2	22
Total	41	100	18.6

The average recurrence interval in relation to the clinical stage of the tumor at the time of original treatment is shown in Table III. It is well known that patients with early lesions have the best prognosis in terms of five-year cure rates. Table III suggests a better prognosis for patients with early tumors, even though uncured, in that they had a longer average interval between treatment and recurrence than did patients with more advanced lesions. Table IV in a similar manner indicates a longer average period of freedom from recurrence in patients with tumors of low than of high histologic grade, just as the cure rate is higher for the former also. Healy and Brown (1939) have demonstrated the best prognosis in endometrial carcinoma, as evidenced by five-year survivals, to be associated with well differentiated tumors; that is, those of low histologic grade. This observation was confirmed in a recent study of the cases treated at the Roosevelt Hospital.

TABLE III. AVERAGE RECURRENCE INTERVAL OF ENDOMETRIAL CARCINOMA ACCORDING TO CLINICAL STAGE

STAGE	CASES	PER CENT	INTERVAL (MONTHS)
Early	7	19	30
Intermediate	10	27	12
Advanced	20	54	16
Total	37	100	

TABLE IV. AVERAGE RECURRENCE INTERVAL OF ENDOMETRIAL CARCINOMA ACCORDING TO HISTOLOGIC GRADE

GRADE	CASES	PER CENT	INTERVAL (MONTHS)
1	11	42	21
2	10	38	16
3	5	19	13
Total	26	99	

In summary, our records show that out of 42 patients with endometrial carcinoma in whom viable tumor cells remained after definitive treatment, regrowth of the residual tumor to a clinically apparent stage occurred in 41 within five years; and in three-fourths of these patients the recurrence was evident within two years. The single case of later recurrence is described below.

CASE 1.—K. H. (R. H. No. 41882), a 56-year-old white private patient of Dr. William P. Healy, had a curettage at another hospital on Nov. 8, 1938, because of postmenopausal bleeding of 5 months' duration. Her last menstrual period had been 6 years previously, at age 50. A sister had died at age 74 with breast cancer. Pathologic report on the curettings was "papillary adenoma malignum" (adenocarcinoma, Grade I) (Fig. 1). The patient was treated with 3,600 mg. hr. of intrauterine radium in corpus tandem. When examined ten months later, she felt well and there was no evidence of neoplastic disease. She remained well and bled no more until eleven days before her admission to the Roosevelt Hospital eight years later, on Jan. 20, 1947, at the age of 64 years. Recent endometrial biopsy was said to have shown adenocarcinoma. The day after admission total hysterectomy, bilateral salpingo-oophorectomy, and appendectomy were performed. The uterus was enlarged to twice normal size and was filled with a yellowish tumor mass which had invaded the myometrium deeply but had not yet penetrated the serosa. Histologic section showed an undifferentiated carcinoma of the endometrium, Grade III. (Fig. 2.)

*Comment.*—This case is interesting because of the long latent period (over eight years) between initial treatment and symptoms of recurrence. The histologic difference between the two tumor specimens suggests the possibility that the second tumor was an independent neoplasm rather than a recurrence of the original one. Although distinctly unusual, such late recurrences of fundal carcinoma are not unheard of. Barrows (1944) reported a case with recurrence nine years after radium therapy; and Suitor (1947) has recently reported a pelvic recurrence eleven years later in a patient who had a total hysterectomy (without removal of the adnexa) and postoperative x-ray treatment for corpus cancer.

GROUP 2.—In this group were three patients who received inadequate intrauterine irradiation for endometrial cancer in the mistaken belief that the lesion was benign. With the return of symptoms the carcinoma was discovered two to five years later.

CASE 2.—V. A. (R. H. No. 14028 and No. 15881), a 72-year-old white woman with three children, was admitted for curettage on Dec. 14, 1925, because of a bloody vaginal discharge which she had had for four weeks. Spontaneous menopause had occurred at age 40. Pathologic report on the curettings was endometrial hyperplasia and the patient was treated with 500 mg. hr. of intrauterine radium. Additional sections of the same curettings were cut several years later by Dr. H. C. Taylor, Jr. (1932), who discovered a region of papillary adenocarcinoma, Grade I. The patient was asymptomatic for two years after treatment, when she returned (Nov. 4, 1927) with a recurrent bloody discharge. Curettage at this time revealed Grade I adenocarcinoma. Accordingly, total hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus was normal in size and contained two small papillary tumors of the endometrium with no demonstrable invasion of the myometrium.

*Comment.*—This tumor, of low-grade malignancy, underwent little growth over a period of two years. Progress of the tumor was probably impeded to some extent by the small dose of radium which the patient received.

CASE 3.—E. L. (R. H. No. 13953, No. 15343, and No. 18303), a white spinster of 57 years, was admitted for curettage on Nov. 7, 1925, because of recent postmenopausal bleeding. Her periods had ceased at the age of 53 years. Although the curettings were diagnosed as hyperplasia of the endometrium, restudy several years later (Taylor, 1932) led to a change in diagnosis to adenocarcinoma, Grade 1. The patient was treated with 600 mg. hr. of intrauterine radium. When she returned on May 20, 1927, with a recurrence of the bleeding, another curettage was performed, but the diagnostic error was repeated and intracavitary radium was reapplied for only 900 mg. hr. After freedom from symptoms for three years the patient returned on June 24, 1930, bleeding again. Operation this time consisted of hysterectomy and bilateral salpingo-oophorectomy. The entire endometrium was invaded by a diffuse, well-differentiated adenocarcinoma with the same histologic characteristics as the tumor in the original curettings. There was minimal involvement of the myometrium.

*Comment.*—The extent to which the progress of the lesion was retarded by the two scrapings of the endometrial cavity and the 2 small applications of radium is uncertain. It is interesting, however, that the tumor remained in an early clinical stage for almost five years.

CASE 4.—A. P. (R. H. No. 36210), a 54-year-old white woman with three children, had a curettage at another hospital on Jan. 13, 1944, because of menometrorrhagia. Although the curettings showed atypical glandular hyperplasia and an area of adenocarcinoma, the only treatment given the patient was 2,200 mg. hr. of intrauterine radium. Her bleeding stopped, only to recur two years later, three weeks before admission to the Roosevelt Hospital on Feb. 4, 1946. The curettings obtained at this time were diagnosed as adenocarcinoma, Grade I. When the uterus was removed, sections showed only slight invasion of the muscle wall, but metastatic tumor was present in the right ovary.

*Comment.*—The growth of this tumor over a two-year period was interrupted only by a curettage and inadequate irradiation. Although histologic section of the fundus indicated only slight invasion of the myometrium by carcinoma, metastatic tumor had taken hold already beyond the limits of the uterus.

In each of the three cases in this group, growth of the endometrial cancer continued at a sufficient rate, following intrauterine irradiation, to cause a recurrence of symptoms and thereby to make its presence known within five years. Although in Case 2 the tumor was still in an early clinical stage after four years eight months, in Case 3 ovarian metastasis occurred within two years. Scheffey (1942) has suggested that intracavitary radium, as used to control bleeding of benign origin, may actually retard malignant growth. Two of his patients with corpus cancer had been treated seven and twelve and one-half years previously with 2,400 mg. hr. and 1,200 mg. hr. of intrauterine radium, respectively. Review of the original curettings, which had been interpreted as benign lesions, led to a revision of the diagnosis to carcinoma in each case. Whether the secondary tumors were recurrences or new growths must remain an open question. There is suggestive evidence that radiant energy itself may be carcinogenic for the endometrium.

GROUP 3. This group comprises three cases in which carcinoma of the endometrium was present but was not diagnosed at the time of initial curettage. The patients received no further treatment until the carcinoma became clinically evident at later dates. In one case, in which two and one-half years had elapsed, the lesion, a Grade I adenocarcinoma, was still in a clinically early stage, being confined to the endometrium. In the second case, the tumor, a Grade II papillary adenocarcinoma, was discovered three years after the initial curettage. During the interim it had metastasized to one ovary and the omentum. The third case is reported in detail because of its unusually slow growth.

CASE 5.—M. T. (R. H. No. 4352 and No. 18610), an unmarried white woman of 45 years of age, had a curettage on June 15, 1914, because of metrorrhagia. The following is an excerpt from the pathologic report:



"The tissue consists of a papillomatous overgrowth of the endometrium which is made up of closely placed, dilated, and tortuous acini, the individual cells of which are quite regular. Very little stroma can be seen, there being just enough to act as a superstructure for the epithelium. There is no positive evidence of malignancy but this type of growth possibly may become so."

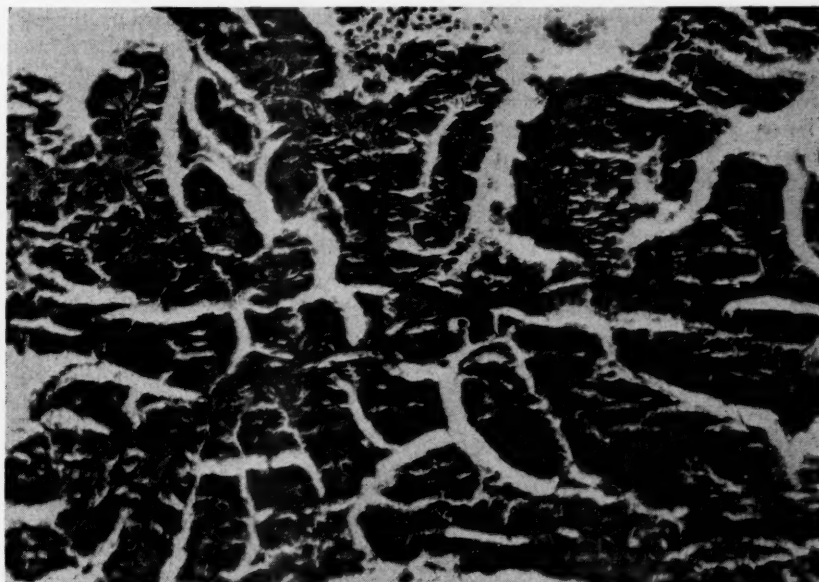


Fig. 1 (Case 1).—Curettings showing adenocarcinoma of endometrium, Grade I.

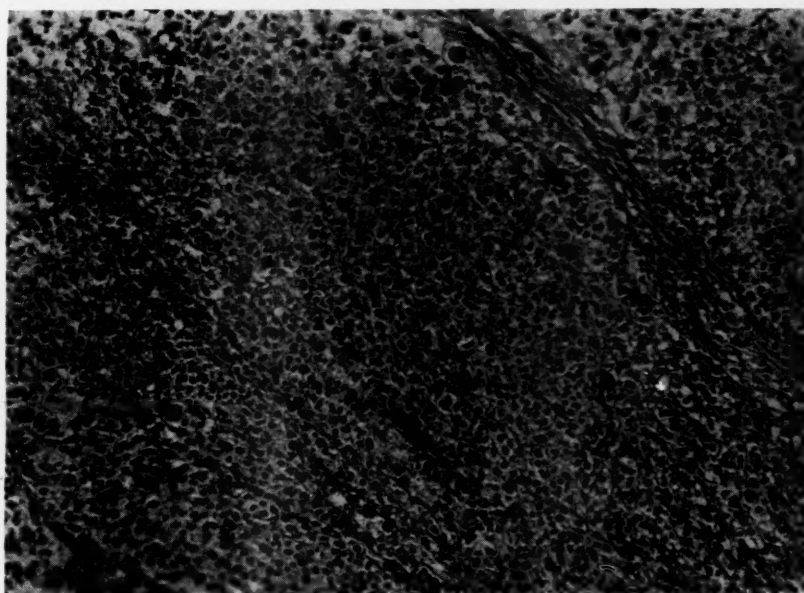


Fig. 2.—Same case, eight years later. Adenocarcinoma of endometrium, Grade III.

The section was reviewed later by Dr. H. C. Taylor, Jr. (1932) who diagnosed the lesion as a typical Grade I adenocarcinoma. Although the history is lacking in detail, the patient apparently flowed off and on from 1914 to 1930, when she was readmitted to the hospital, at age 61, sixteen years after the original curettage. The uterus was small but

contained a large polypoid growth which protruded through the external os. Biopsy of this tumor on Oct. 20, 1930, showed an adenocarcinoma, Grade II.

*Comment.*—Although impossible of proof, the fact that the patient continued to bleed intermittently between her two hospital admissions strongly suggests her having harbored the same uterine tumor for over sixteen years. So slow a rate of growth is extraordinary for untreated endometrial cancer, and this is perhaps the longest history of its kind on record. Taylor's paper of 1932 included two other cases of carcinoma of the endometrium with histories of possibly fourteen and fifteen years, but the early existence of these tumors is questionable since curettage had not been performed.<sup>3</sup>

### Discussion

The time required for the clinical recognition of a tumor's recurrence is the resultant of several factors. Among these are the diligence and diagnostic aids used in the search for the tumor, the vital organs encountered by it in the course of its spread, and its rate of growth. There is little, if any, evidence for a fundamental difference in actual rate of growth between uterine tumors of cervical and those of endometrial origin. They grow at an accelerated tempo during the stages in which they are clinically recognizable. Although rare instances of recurrence after periods of over fifteen years have been noted for both types, the overwhelming majority of unsuccessfully treated ones become manifest within five years and usually within two years. In their incipiency, on the other hand, both cervical and endometrial lesions may advance quite slowly. Taylor and Guyer (1946) have recently reported a seven-year history in a case of early cervical cancer. In two recent cases at the Roosevelt Hospital, almost six years elapsed between the recognition of an atypical hyperplastic change in the endometrium and its development into a clinically and pathologically early malignancy.

### Summary

1. In 41 out of 42 unsuccessfully treated cases of endometrial carcinoma, recurrence of the tumor was observed within five years. Half of the recurrences were noted within the first year of treatment and three-fourths within the first two years.
2. Two unusual cases of corpus cancer are reported, with histories of eight and sixteen years.
3. Preoperative radium irradiation of the uterus in surgically treated cases neither improved the five-year cure rate nor prolonged the interval of tumor recurrence.
4. Tumors in an early clinical stage of development when treated recurred later than did those in more advanced stages.
5. Tumors of low histologic grade recurred later than the less differentiated ones.

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## A METHOD OF FORCEPS ROTATION IN POSTERIOR POSITIONS

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THE Scanzoni maneuver, the Bill modification of the Scanzoni operation, and manual rotation of the head have been the most widely applied methods of rotation of the head in persistent posterior positions. Occasionally, it is feasible to extract the head by forceps without rotation.

To the uninitiated, rotation with forceps by the Scanzoni method is not without the danger of damage to the maternal soft parts because of the tightness of these parts at the plane at which the rotation is done. In rotation done manually, the head is usually dislodged, and, although it occurs infrequently, prolapse of the cord is a constant threat. Also, with manual rotation of the head, not infrequently the head cannot be sufficiently fixed to prevent conversion to the original posterior position before, or when, the forceps blades are applied. However, the danger of soft tissue damage, when manual rotation is done, is minimal. Since there is so little trauma with manual rotation, the method of forceps rotation of the posteriorly placed head by upward dislodgment prior to rotation was conceived.

Nonfenestrated blades of the Tucker-McLean type with long shaft and with the cephalic portion extending from the shaft at about a 30-degree angle are used, since the head is usually incompletely flexed in the posterior position. The station of the head above or below the spines, or on the pelvic floor, does not preclude the use of this method. All the tenets pertaining to the use of forceps must be followed, i.e., complete dilatation of the cervix, or as complete dilatation as can be obtained with posterior positions, ruptured membranes, an adequate cephalopelvic relationship, and an empty bladder. In addition, though not an absolute necessity, a level of anesthesia should be used that will give proper degree of relaxation of the uterus but not to the degree required for version and extraction. This method of rotation has been done under gas-oxygen-ether, cyclopropane, spinal, caudal, and Delvinal supplemented with gas-oxygen anesthesia.

It is best that the patient's buttocks should hang over the edge of the delivery table slightly. The reason for this precaution will be self-evident.

After the position has been accurately determined, the first application of forceps is made, exactly as in the Scanzoni maneuver, i.e., if the position is found to be right occipitoposterior, the Tucker-McLean forceps are applied for a left occipitoanterior position, with the pelvic curve of the forceps directed toward the baby's face, if occipitoposterior for occipitoanterior, etc. (Fig. 1.) It is absolutely essential that the forceps be closely applied to the head and be inside the cervix, when complete retraction of the cervix has not been effected. The handles of the forceps should lock easily and accurately. The handles of the forceps are then pushed back toward the table at about a 45-degree angle with the floor. As this is done, the shaft is pushed gently upward into the pelvis. At this point, the shaft pushes against the perineal body. As the upward thrust is begun and the head is dislodged above the spines, the handles of the forceps are rotated on their axis, clockwise in a right occipitoposterior position, counterclockwise in a left occipitoposterior position (Fig. 2 and Fig. 3). The backward push, upward thrust of the shaft, and rotation of the blades are actually one gentle, coordinated movement. Minimal exertion of force is necessary. In performing this procedure, the head is swung around in the wide arc, whereas the

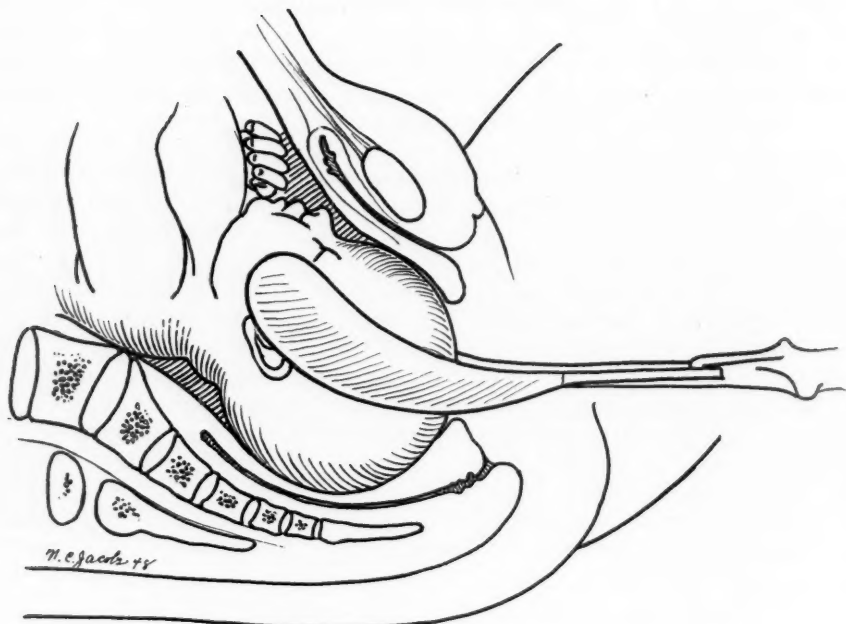


Fig. 1.—Original application of forceps for the posterior position.

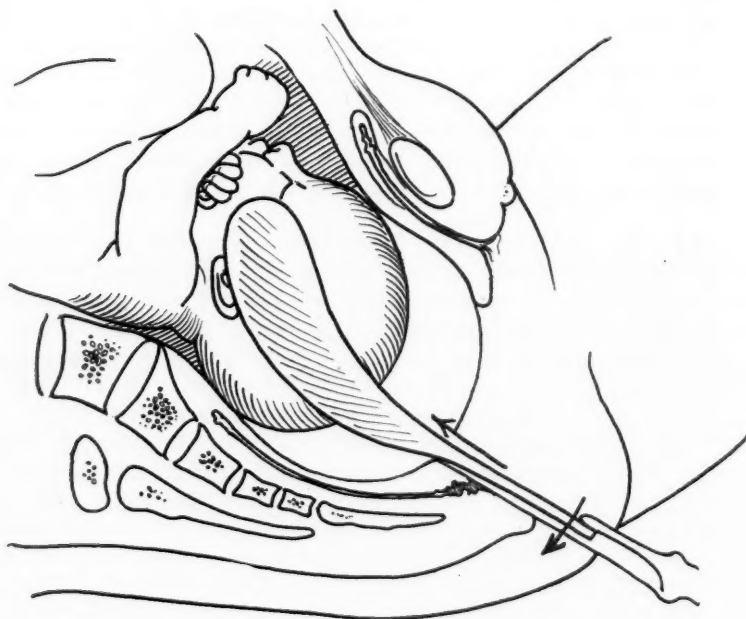


Fig. 2.—Downward and backward depression of the forceps handles with upward dislodgment of the head.



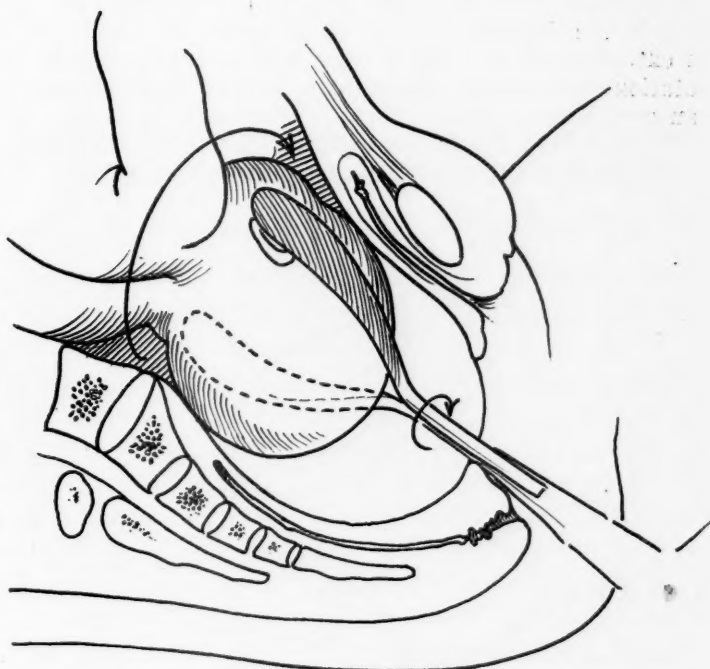


Fig. 3.—Rotation of the head. *Note.*—b and c, though represented separately, are one coordinated movement.

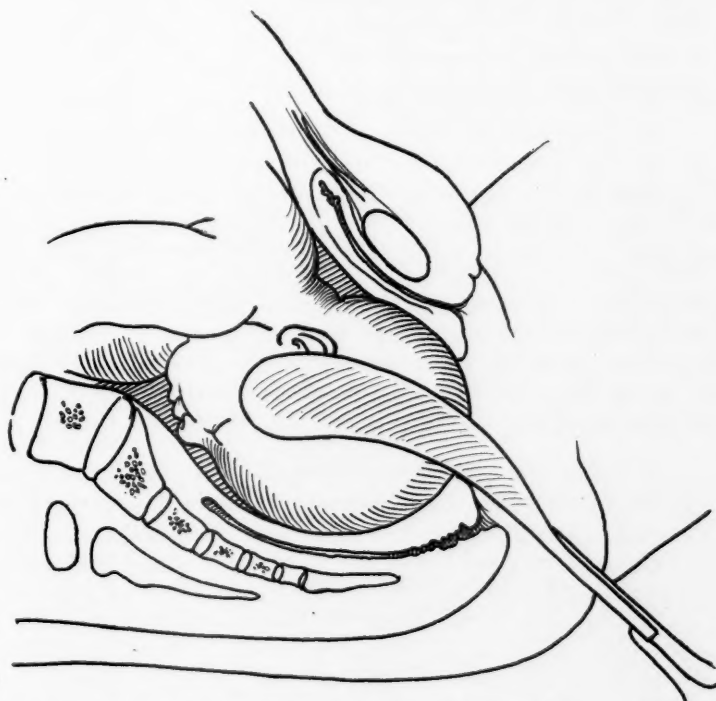


Fig. 4.—Head has been pulled deep into pelvis with forceps inverted.

handles of the forceps rotate on their axis in a small arc; the opposite of the procedure used in the Scanzoni operation. Frequently, the head completes the rotation with extremely little tension, once the rotation is gently started.

When rotation from occipitoposterior is desired and the original position is not known, an exploratory gentle effort at rotation to the right or left may be attempted. Almost invariably the head will rotate to the original position, right occipitoposterior or left occipitoposterior, with greater ease than to the opposite position.

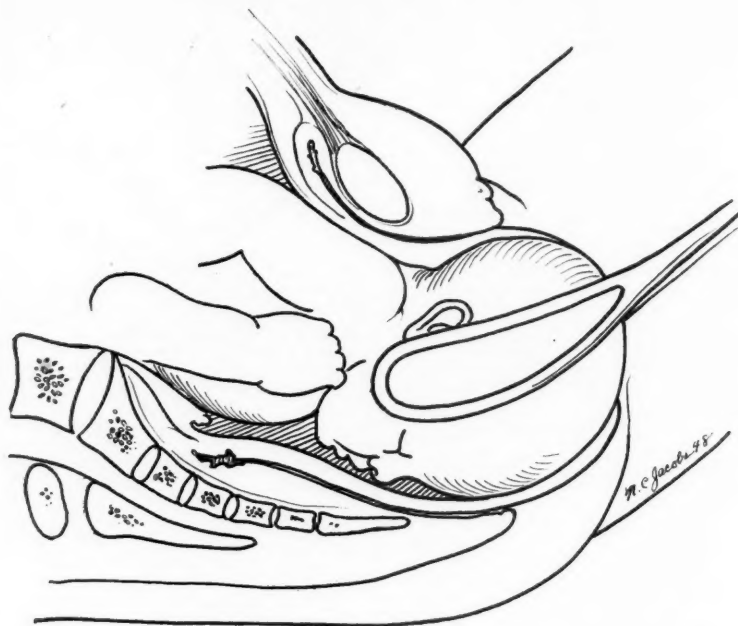


Fig. 5.—Second pair of forceps applied.

When the head has been completely rotated to occipitoanterior position through the 135 to 180 degree arc, it is pulled well down into the pelvis (Fig. 4). While pressure is exerted on the fundus, the inverted blade that is to be replaced in the anterior position is removed first, i.e., if the original position had been left occipitoposterior, the blade to be removed from the left side of baby's head and mother's pelvis will be replaced first. The second blade is removed after the first blade has been replaced. The McLean-Tucker forceps have been replaced by DeWees, Elliotts, Simpsons, or Tarniers in the second application. The remainder of the forceps delivery is completed in the usual manner (Fig. 5).

The time of doing the episiotomy is optional. We have found it more desirable to do the episiotomy, usually of the mediolateral type, after the rotation has been completed and the forceps reapplied. We feel that extension of the episiotomy into the vaginal sulci is less apt to occur if the episiotomy is done late.

The method has many advantages: 1. there is little trauma to the vaginal mucosa and its underlying fascia since the head has been rotated high in the pelvis or at the pelvic brim; 2. the rotation is well controlled, more so than by manual rotation; 3. in the case of prolapse of the cord, which we have seen very rarely, there is little danger to the baby, since the delivery is usually completed within a few minutes after rotation has been completed.

## A NEW CONCEPT IN THE REPLACEMENT OF THE INVERTED UTERUS AND A REPORT OF NINE CASES\*

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IT IS the purpose of this paper to describe the method used in replacing the inverted uterus to its normal position, and to report nine such cases. This method of replacement was successful in all.

Several operations have been devised to correct the inverted uterus. The method to be described does not require any surgical procedure, and may be called "manual replacement." The uterus cannot be replaced by dimpling or making pressure on the fundus uteri or by any procedure in which the uterus is allowed to remain in the pelvis. The uterus must be lifted into the abdominal cavity above the level of the umbilicus, at which time the passive action of the uterine ligaments corrects the malposition. The entire procedure depends upon this action of the uterine ligaments. Therefore attention is called (Fig. 1) to the origin and insertion of these ligaments; namely, the round, broad, uterosacral, and uterovesical. Fig. 2 shows the ligaments as they appear in an inverted uterus when the uterus is in the pelvis. The ligaments are not altered in tension or length by the inversion of the uterus per se. To replace the inverted uterus the entire hand is placed in the vagina with the tips of the fingers at the uterocervical junction and the fundus uteri in the palm of the hand. The entire uterus is then lifted out of the pelvis and forcefully held in the abdominal cavity above the level of the umbilicus. It is shown in Fig. 3 that all the uterine ligaments are stretched and very tense because the distance between the origin and insertion of the ligaments is greatly increased by this maneuver. This is in contrast to the relaxed and unaltered condition of the ligaments when the inverted uterus is in the pelvis. The ligaments are so situated that, when they are placed under tension, pressure is exerted first to widen the cervical ring, second to pull the fundus through it, and thereby replace the uterus to the normal position. It is necessary to hold the uterus in this position for a period of three to five minutes, at which time the fundus recedes from the palm of the hand, as shown in Fig. 4. It is emphasized that in order to accomplish this procedure the entire hand and two-thirds of the length of the forearm must be placed in the vagina, otherwise the pull and tension of the ligaments are not sufficient to correct the condition.

CASE 1.—G. K. (St. Joseph Hospital), a white multipara, para ii, gravida iv, aged 26 years, was admitted on Mar. 12, 1931. The antepartum course and previous history were uneventful. A spontaneous delivery of a living female child in the occiput posterior position occurred at 4:28 A.M. on March 12. The placenta was delivered intact twenty minutes later followed by a profuse hemorrhage. Morphine,  $\frac{1}{4}$  grain, oxytocics, 1,000 c.c. of saline, and 600 c.c. of blood were administered. She was discharged on the sixteenth day in good

\*Presented at a meeting of the Brooklyn Obstetrical Society, March 5, 1948.

condition. Approximately three months later she visited her family physician because of vaginal bleeding following intercourse, and an inverted uterus was found. Upon readmission to the hospital on June 3, 1931, her general condition was excellent and the blood count normal. Two days after admission, the uterus was replaced manually under gas-oxygen anesthesia. The cervix was so soft and patulous that three interrupted sutures were placed

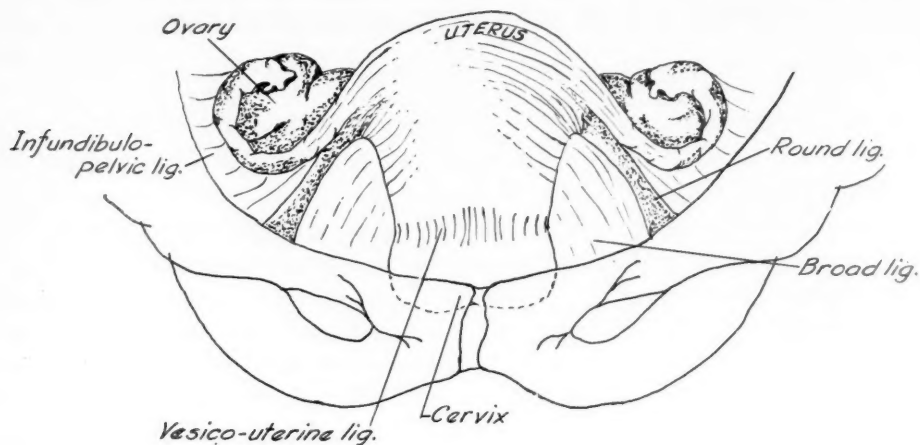


Fig. 1.

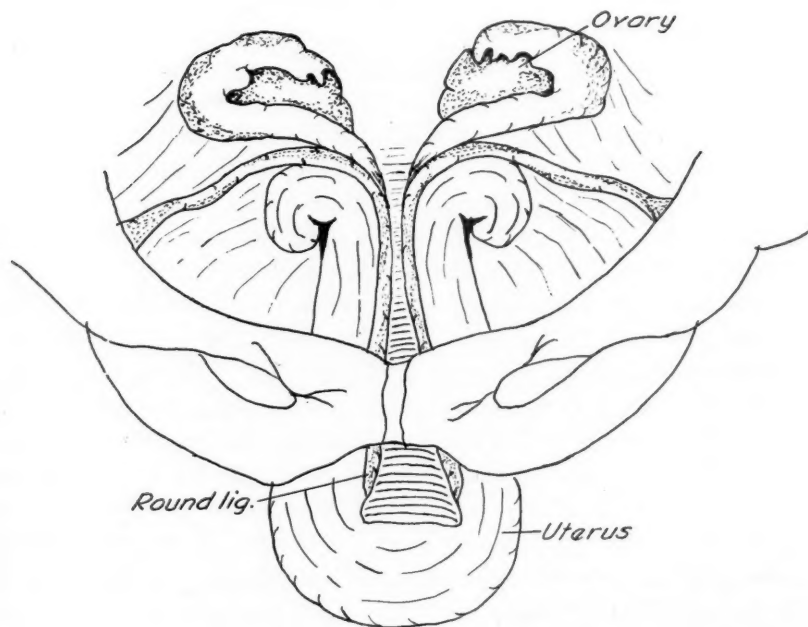


Fig. 2.

through the lips of the cervix with the idea of preventing a recurrence. The patient made an uneventful recovery without fever or symptoms, and was discharged eight days after reposition of the uterus. Two months later examination by her physician revealed the uterus in good position and condition. In 1937 an operation was performed for salpingitis, and the uterus was found to be in good position.



CASE 2.—G. K. (Rockaway Beach Hospital), a white primipara, aged 19 years, was admitted June 20, 1936. Previous history and prenatal history were uneventful. After about fourteen hours of labor at 4:30 P.M., the patient was delivered of a living female child by means of low forceps. A second degree laceration was repaired. After many attempts and an excessive amount of Credé, the placenta and membranes appeared at the vagina thirty-one minutes after delivery. The placenta was removed from the vagina with much difficulty, followed by profuse bleeding for which the vagina was packed. The patient was placed in Trendelenburg position, given 500 c.c. of glucose intravenously, morphine, and oxytocics.

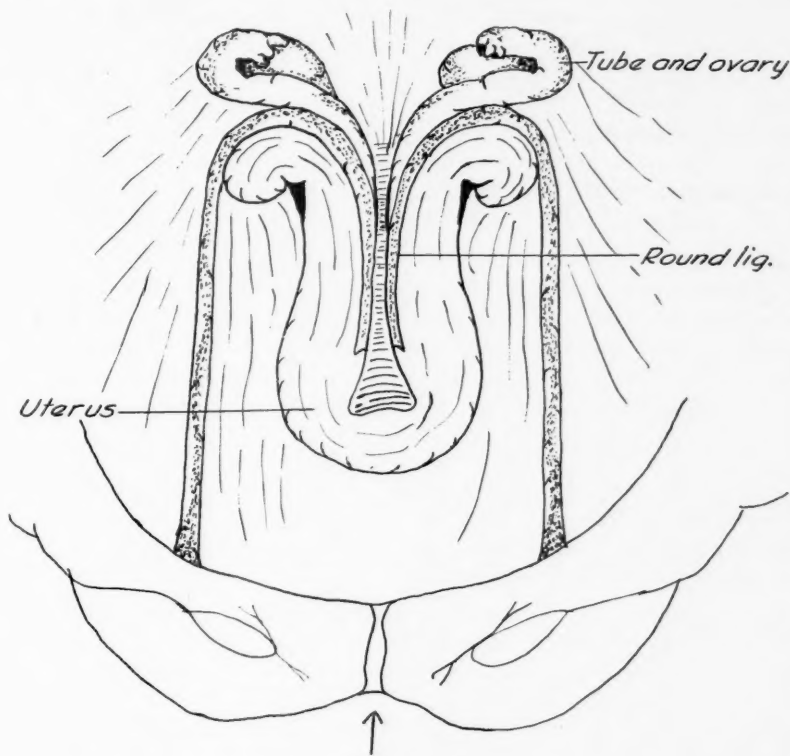


Fig. 3.

Bleeding continued in spite of packing. I saw this patient at 4:30 A.M., on June 21, approximately eleven hours after delivery. She was in severe shock, pulse 150, blood pressure 40 and at 5:30 A.M., 500 c.c. of blood were given. At 5:40 A.M. the vaginal packing was removed and an inversion of the uterus was revealed. Under gas oxygen anesthesia an attempt was made to reduce it. This was unsuccessful, and the vagina was packed with mercuriochrome soaked gauze. For the next ten days the patient's condition was not good: vaginal bleeding moderate, red blood count 1,920,000, hemoglobin 34 per cent, temperature ranged from 100 to 104° F., marked abdominal distention, severe abdominal cramps, and catheterization was necessary. During this period two more transfusions were given, totaling 1,210 c.c. From the tenth to the fourteenth day her general condition improved and the temperature was normal. On the fourteenth day post partum under gas oxygen anesthesia the uterus was replaced. A suture was also placed through the cervical lips in this case. For the next week the patient had a temperature ranging from 103° F. to normal, after which time it remained normal. On the twenty-fifth day post partum, the blood count was normal, and upon vaginal examination there were no abnormal findings. On August 18, six weeks post partum, vaginal examination was negative except for an eroded cervix which was treated by cauterization. She has since been delivered of a baby with no difficulties during the third stage of labor.

CASE 3.—D. T. (St. Joseph Hospital), a white multipara, para i, gravida ii, aged 30 years, was admitted in active labor at 12:30 P.M., Feb. 2, 1939. Her previous pregnancy and history were uneventful. She had been in labor for about an hour and a half before admission. After an episiotomy was performed, the spontaneous delivery of a living male child occurred at 1:20 P.M. Under ether anesthesia the episiotomy was repaired. Several attempts were made to express the placenta. There was practically no vaginal bleeding. Twenty minutes after delivery more than the usual amount of pressure was exerted upon the fundus. The

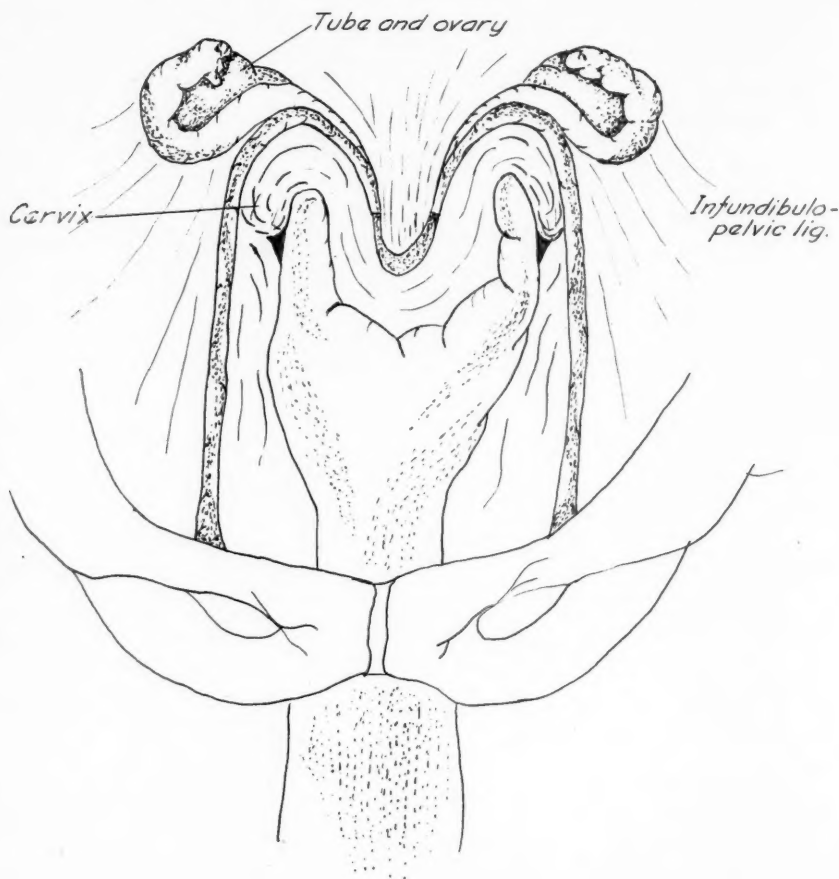


Fig. 4.

placenta appeared at the introitus in the manner of an inverted umbrella. It did not separate and was removed manually. During the removal, the placenta was found to be adherent to an inverted uterus. I was unable to determine whether or not the placenta was attached at the fundus; however, it appeared to be. During this time the patient was coming out of the ether anesthesia. There was no evidence of shock, and bleeding was about 100 c.c. She was immediately anesthetized with ether, and the uterus was repositioned. The vagina was packed with iodoform gauze. Her condition was good, blood pressure 80/50, pulse 126. The vaginal packing was removed five hours later, and the postpartum course was uneventful. She was discharged on the tenth day in good condition; vaginal examination revealed no abnormalities. Six weeks post partum, the uterus was in good position and condition. This patient was delivered again on Jan. 30, 1948, uneventfully.

CASE 4.—H. R. (South Nassau Communities Hospital), a white primipara, aged 25 years, with an uneventful previous history, was admitted April 7, 1939. After a fourteen-hour labor

a living male child was delivered at 10:55 P.M. by low forceps under ether anesthesia. One ampule of ergotrate was given, and the perineum repaired. Twenty minutes later, after several attempts and marked pressure upon the fundus, the placenta presented itself at the introitus in an inverted umbrella fashion, and was removed from the vagina manually. During this removal it was found to be adherent to an inverted uterus. Profuse bleeding followed, and 1,000 c.c. of 100 per cent glucose were given intravenously. Many attempts were made to reduce the inversion, during which time the patient was under ether anesthesia, and the bleeding was profuse. I saw this patient about one hour after delivery. Her condition was poor, and she was still under anesthesia. The uterus was replaced manually and packed with gauze. The anesthesia was stopped, and ergotole and morphine were given. The patient was very restless and was moving around the table; her pulse very rapid, and her blood pressure was not obtainable. Oxygen was administered because of the marked cerebral anoxemia. Following a blood transfusion of 450 c.c. her condition improved. The next day, the pulse was still very rapid, there was marked pallor, and general condition poor. Another transfusion of 700 c.c. was given, and the uterine packing was removed. For the next five days the temperature remained between 100° and 102° F. Vaginal bleeding was moderate, and her general condition improved. She was discharged twelve days post partum in good condition, the uterus being anterior and well involuted.

CASE 5.—A. P. (South Nassau Communities Hospital), a white primipara, aged 23 years, was delivered by breech extraction at 3:34 A.M., Aug. 8, 1942, after twenty-nine hours of labor. The placenta was delivered without difficulty at 3:44 A.M. The patient bled profusely, was pulseless, and her blood pressure was 60/0. Plasma was given and the uterus was packed with iodoform gauze. Fifteen hundred cubic centimeters of plasma and 700 c.c. of blood were given. The condition improved very nicely, the packing was removed in thirty-six hours, and she was discharged on the twelfth day after delivery. Moderate bleeding continued after discharge from the hospital, and on Oct. 8, 1942, two months post partum, I saw this patient and examination revealed an inverted uterus. She was admitted to the hospital and the uterus was replaced. Temperature was 102° F. for twenty-four hours, then returned to normal. She was discharged in good condition five days after replacement.

CASE 6.—V. B. (South Nassau Communities Hospital), a white multipara, para i, gravida ii aged 28 years, was admitted on Feb. 5, 1943. After twenty-five hours of poor labor a living child was delivered by low forceps at 11:42 P.M. on Feb. 6, 1943. One hour and ten minutes later, after much difficulty, the placenta was delivered. I saw this patient at 2:00 A.M., at which time she was in severe shock. The vagina had been packed and there was slight bleeding present. One thousand cubic centimeters of plasma and 500 c.c. of glucose were given, and at 3:00 A.M., her pulse was improved and blood pressure 90/60. At 5:00 A.M., 700 c.c. of blood were given, the patient continued to bleed, and at 6:35 A.M. gas-oxygen anesthesia was administered, the packing removed, and the uterus found to be inverted. The uterus was replaced and packed. Five hundred cubic centimeters of plasma and 1,300 c.c. of blood were given during the next eighteen hours. Packing was removed in twenty-four hours, temperature 103° F., pulse rapid but good quality, and moderate abdominal distention existed. Temperature after five days became normal. Sulfathiazole was given during this period. The patient was discharged fifteen days post partum in good condition.

CASE 7.—S. E. (South Nassau Communities Hospital), a primipara, aged 23 years, was admitted on Dec. 22, 1944. The patient was delivered at 3:42 P.M. by forceps after ten hours' labor. At 5:55 P.M. the placenta was delivered, and was followed by a hemorrhage of about 1,500 c.c. I saw this patient at 7:30 P.M. in severe shock. Plasma was being given at the time and a total of four pints was administered. At 8:15 P.M. moderate bleeding was present, blood pressure 72/0. Vaginal examination revealed an inverted uterus. Gas-oxygen anesthesia was given, and the uterus was replaced and packed. At 8:45 P.M. the blood pressure was 72/0, pulse 136, and plasma was still being administered, the last of the fourth pint. Uterine packing was removed in thirty-six hours, and 500 c.c. of blood were given. The patient had a temperature of 101° to 102° F. for five days, and was discharged on Jan. 6, 1945, in good condition, fourteen days post partum.

CASE 8.—I. F. (South Nassau Communities Hospital), a white primipara, aged 28 years, was admitted April 17, 1945. She was delivered at 9:46 A.M. by low forceps after ten hours of labor. At 10:10 A.M. the placenta was delivered intact with a moderate amount of bleeding. At 11:40 A.M. profuse bleeding occurred, the pulse and blood pressure were not obtainable, and plasma was administered. This patient was seen for the first time at 12:15 P.M. by my associate, Dr. George E. Christmann. Vaginal examination revealed an inverted uterus which was replaced and packed under gas-oxygen anesthesia. During this time the patient had received four pints of plasma, and at 3:00 P.M. a pint of blood. The following morning her condition was much improved, the uterine packing was removed, and another pint of blood was given. The patient had a temperature of 101° to 102° F. for four days, and was discharged on the twelfth day post partum in good condition.

CASE 9.—M. G. (St. Joseph Hospital) a white primipara, aged 29 years, was admitted June 20, 1947, and was delivered by low forceps at 4:28 P.M. after twelve hours of labor. At 4:42 P.M. the placenta was delivered intact with a moderate amount of bleeding. At 6:00 P.M. the patient bled more than usual, and intravenous glucose and saline were given. At 7:30 P.M. profuse bleeding occurred, pulse 160 and blood pressure 50/0. Two pints of plasma and one pint of blood were administered. At 7:50 P.M. under gas-oxygen anesthesia, examination revealed an inversion of the uterus which was replaced and packed. At 8:15 P.M. her pulse was 145, blood pressure 90/70, and the patient's condition was fair. Another pint of blood was given. On the following day her condition was good, and the uterine packing was removed. Recovery was uneventful, and the patient was discharged in good condition eight days post partum. Her temperature did not go over 100° F. at any time. Six weeks post partum examination revealed the uterus in good position.

### Summary

A method of manual replacement of the inverted uterus is described.

This method of replacement is simple and can be done immediately without increasing shock. As a matter of fact, shock and hemorrhage are relieved by this procedure.

General anesthesia is necessary and was used in all cases.

Nine cases of inversion of the uterus are reported.

Six cases or 67 per cent were primiparae.

The ages ranged from 19 to 30 years.

All cases but one showed marked shock and hemorrhage. These cases required from one pint of blood to as much as four pints of blood and three pints of plasma. One case was diagnosed immediately and the uterus was replaced within six minutes after inversion. There were no signs of shock or hemorrhage and further treatment was unnecessary on this patient.

In seven cases the third stage of labor lasted thirty-one minutes or less, in one case seventy minutes, and another two hours and thirteen minutes.

In six cases the period of inversion was short, varying from six minutes to five hours and thirty-five minutes. In one case the period of inversion was fourteen days, in another two months, and in a third, three months.

In two cases subsequent pregnancies were uneventful.

1502 MOTT AVENUE



## ROENTGEN DIAGNOSIS OF ADENOMYOSIS UTERI

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**A**DENOMYOSIS of the uterus is a condition characterized by benign invasion of the endometrium into the uterine musculature associated with an overgrowth of the latter.<sup>1</sup> It differs from pelvic endometriosis in that whatever is responsible for the abnormal endometrial growth affects the uterine musculature as well. On section through such a uterus, the striking feature is this marked musculature overgrowth. A frequent, although not constant, feature on examination of the extirpated uterus is the presence of dark, hemorrhagic areas varying in size from 1 to 4 mm. in diameter and scattered discretely throughout the musculature. The latter represent islands of endometrium in which menstrual hemorrhage has occurred. This invasion of endometrium into muscle forms tubelike structures into which the radiopaque media may penetrate, producing according to our findings a rather characteristic roentgen film. Short, spiculelike structures extend especially from the superior surface of the uterus varying in size from 1 to 4 mm. and ending in very tiny sacs. This roentgen finding was noted in approximately 15 per cent of the cases of adenomyosis. A possible cause for failure of the dye to enter the endometrial channels in the other cases is the marked overgrowth of muscle which may act as a pinch-cock preventing the dye from going into the endometrial channels. Another possible cause for failure is the presence of clotted blood within the endometrial channels. We have made the diagnosis of adenomyosis by the above means twelve times in a series of three hundred hystero-grams performed because of menstrual irregularity. These cases were confirmed by hysterectomy.

Some of the cases of adenomyosis found at operation which did not reveal the tiny sacs on review of the roentgenograms revealed an irregularity of the uterine border. This irregularity was more marked than was usually noted with hyperplasia of the endometrium. On pelvic examination, the uterus in these cases was usually globular and slightly enlarged. These findings would therefore suggest adenomyosis when the tiny sacs were not visualized. Adenomyosis can, on occasion, produce a filling defect within the uterus which simulates a submucous fibroid. Two such cases were encountered. The uterine walls, in these cases, were unusually thick and probably only permitted the dye to outline the periphery of the uterine cavity. Recently we have visualized the tiny sacs more frequently. A possible explanation may be the use of Skiodan acacia in preference to Lipiodol. Skiodan acacia is less viscous and probably enters the endometrial channels more readily than Lipiodol.



Fig. 1.—Uterine cavity is normal in size, shape, and position. There is no evidence of any filling defects. Several tiny sacs are seen extending from the superior surface of the uterine cavity. *Impression:* adenomyosis uteri.



Fig. 2.—The uterine cavity is normal in size, shape, and position. Several small projections are seen extending from the left side of the uterine cavity. *Impression:* adenomyosis uteri.

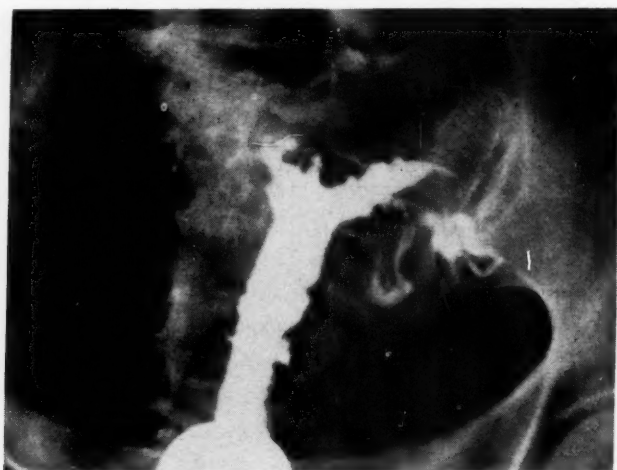


Fig. 3.—The uterine cavity is normal in size, shape, and position. There are several large sacs extending from the superior surface of the uterine cavity. Others are seen immediately above the cervical os. *Impression:* adenomyosis uteri.

### Case Reports

CASE 1.—S. H., a 40-year-old woman, entered Mount Sinai Hospital with a chief complaint of profuse menstrual bleeding lasting eight to nine days and passing clots. Her present illness started six months ago with an increase in her periods. Her last two periods were very severe, lasting ten days and passing numerous clots. The remainder of the history was essentially negative.

*Physical examination:* The uterus was slightly enlarged, not tender. Both adnexa were not palpable. The cervix was not smooth. The remainder of the physical examination was negative. Hysterography revealed no evidence of any filling defects. Several tiny sacs were seen extending from the superior surface of the uterine cavity. A diagnosis of adenomyosis was made which was confirmed by the pathologic sections (Fig. 1).

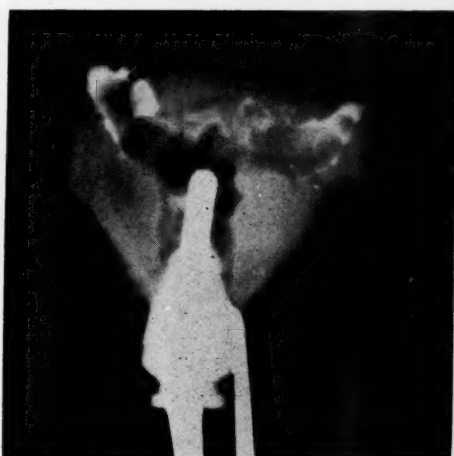


Fig. 4.

Fig. 4.—Same case as above, revealing the sacs in the injected specimen.



Fig. 5.

Fig. 5.—Hysterography reveals the uterine cavity to be normal in size, shape, and position. Several sacs are seen extending from the uterine border.

CASE 2.—M. P., was a 36-year-old woman with the chief complaint of dysmenorrhea and menorrhagia of many years' duration. Pelvic examination disclosed an enlarged, globular uterus the size of an orange. Both adnexa were thickened and not tender. Numerous small nodules were palpated in the cul-de-sac. Hysterography revealed many small projections extending from the left side of the uterine cavity. A diagnosis of adenomyosis was confirmed by the pathologic sections (Fig. 2).

CASE 3.—L. F. was a 43-year-old woman with the chief complaint of dysmenorrhea since the onset of her periods and menorrhagia during the last four years. Pelvic examination disclosed the uterus to be enlarged to a two months' gestation due to multiple fibroids. Hysterography revealed several large sacs extending from the superior surface of the uterine cavity. Others were seen immediately above the cervical os. Hysterectomy and sections confirmed the diagnosis of a fibroid uterus with adenomyosis (Fig. 3). Fig. 4 reveals the sacs in the injected specimen.

CASE 4.—T. L. was a 32-year-old woman with the chief complaint of menorrhagia of six months' duration. Pelvic examination revealed the uterus to be enlarged to the size of a three months' gestation by multiple fibroids. Hysterography revealed several tiny sacs extending from the uterine border. (Fig. 5). One fairly large sac was seen above the cervical os on the right side. Hysterectomy and section confirmed the above diagnosis.



Fig. 6.—The uterine cavity is normal in size, shape, and position. Several small sacs extend from the superior surface of the uterine cavity.



Fig. 7.—The uterine cavity is small. There is a concavity on the superior surface of the uterine cavity which can be due to an intramural fibroid but which is occasionally seen normally. Several small sacs are seen extending from the superior surface of the uterine cavity.

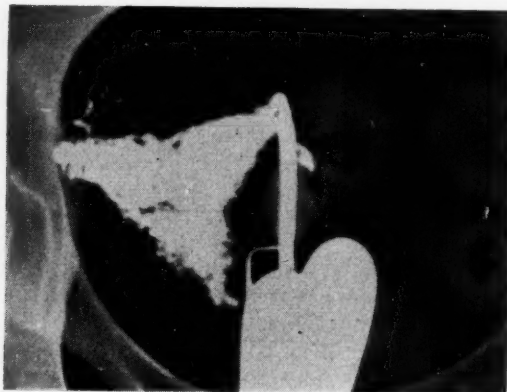


Fig. 8.—The uterine cavity is slightly enlarged, dextroverted. There are several small filling defects within the uterine cavity and tiny sacs extending from the border of the uterine cavity. *Impression: adenomyosis.*



CASE 5.—A. S. was a 36-year-old woman with the chief complaint of dysmenorrhea and a feeling of weight in her pelvis. Her periods were normal. Pelvic examination revealed the uterus to be enlarged to the size of a grapefruit. Hysterography revealed several small sacs extending from the superior surface of the uterine cavity (Fig. 6). Operation confirmed the diagnosis.

CASE 6.—R. R., a 48-year-old woman, was admitted with abdominal pain, menorrhagia, dysmenorrhea, and anemia. The uterus was enlarged and nodular. Endometrial biopsy revealed a proliferative endometrium. Hysterography revealed several tiny sacs in the superior portion of the uterine cavity (Fig. 7). Dilatation and curettage were done and the pathologic report revealed fragments of endometrium in a proliferative stage. She was admitted again one year later with a severe metrorrhagia for two months after four months after amenorrhea. Pelvic examination was similar to the previous admission. Hysterectomy was performed which revealed adenomyosis and small fibromyomas.



Fig. 9.—The uterine cavity is normal in size, shape, and position. A circular filling defect is noted within the uterine cavity. At operation, this was found to be due to thickened uterine musculature rather than to submucous fibroid.

CASE 7.—L. G., a 42-year-old woman, was admitted with the chief complaint of vaginal spotting for the last six weeks. Pelvic examination revealed the uterus to be slightly enlarged. Hysterography performed with Lipiodol revealed several tiny sacs extending from the border of the uterine cavity. In addition, numerous small filling defects were seen within the uterine cavity. Hysterectomy revealed adenomyosis (Fig. 8).

CASE 8.—S. A., a 28-year-old woman, was admitted with the diagnosis of menometrorrhagia of two years' duration. Recently the bleeding had become severe and the patient passed numerous clots. Pelvic examination revealed the uterus to be slightly enlarged. Both adnexa were not palpated. Hysterography revealed (Fig. 9) a filling defect occupying practically the entire uterine cavity. A diagnosis of a submucous fibroid was made. Dilatation and curettage were performed and, although the operator could feel a tumor, he was unable to remove it. Hysterectomy revealed a uterus that was slightly enlarged. The muscular layer was extremely thickened and bulged into the uterine cavity. Except for a very small endometrial polyp in the left upper quadrant of the uterine cavity, no further abnormality was noted. It was felt that the marked overgrowth of muscle produced a bulging into the uterine cavity which simulated a submucous fibroid. We have since encountered this finding in another case confirmed by operation.

### Conclusions

1. Hysterography is of great help in determining the presence of intra-uterine pathology.
2. Adenomyosis uteri can be occasionally diagnosed by hysterography, especially when the dye enters the endometrial pits which have invaded the uterine musculature.
3. The above findings has been seen more frequently since the use of Skiodan acacia.
4. Hysterography has been very helpful in the institution of more specific therapy.
5. There have been no reactions or ill effects from the use of Skiodan acacia in these cases.

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1075 PARK AVENUE

## THE PROPHYLACTIC USE OF PENICILLIN IN OBSTETRICS

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THE standard of maternal morbidity as set by the American College of Surgeons includes all cases with temperature of 100.4° F. or over for more than twenty-four hours, excluding the first twenty-four hours post partum. This does not include low-grade fevers below this temperature which may, in themselves, be evidence of some serious condition, yet are not included in the standard morbidity rate.

In an endeavor to discover a means to reduce this standard morbidity and at the same time the low-grade fevers mentioned above, a study was made in the Grace Maternity Hospital, Halifax, N. S., using prophylactic penicillin on all postpartum cases delivered by the vaginal route.

These patients were given 20,000 units of calcium penicillin intramuscularly every three hours for ten doses beginning immediately post partum. If the membranes were ruptured for more than twelve hours before delivery, the penicillin was started pre partum. In addition to the above, if the patient did develop a fever, the penicillin was continued as long as seemed necessary.

Four hundred forty-six cases delivered during the months of April, 1947, to January, 1948, both inclusive, received the above dosages of penicillin. The percentage morbidity of these cases was then compared with 457 cases delivered during the corresponding months of April, 1946, to January, 1947, both inclusive, in which no prophylactic penicillin was given. Temperatures were taken every four hours.

In this hospital for several years, there has been an opportunity to study the effects of early rising as compared to those of late rising. During the months of May, July, September, November, and January of both series, the patients were permitted to get up and walk around the bed on the day following delivery. On the alternate months, they did not leave their beds until the sixth day. In addition, the early risers were given a simple series of bed exercises. Reference will be made later in this paper to the effects of early and late rising on the morbidity rates.

TABLE I. INCIDENCE OF CAUSES OF MORBIDITY (OVER 100.4° F.)

	SAPRE- MIA	MAS- TITIS	INFECTED EPISIOT- OMY	PYELITIS	CHEST	PHLE- BITIS	OTHERS	NIL NOTED
No penicillin	13	6	3	8	4	0	1	10
Prophylactic penicillin	6	6	0	6	2	0	1	0

In the months in which there was no prophylactic penicillin used, 45 cases developed a temperature of over 100.4° F. for more than twenty-four hours, giving a gross morbidity of 9.8 per cent. Compare this to the months in which prophylactic penicillin was used, when 21 cases developed the above temperature, giving a gross morbidity of 4.7 per cent. Table I shows that several of these cases were not due to infection in the genital tract, so if we include only those cases associated with lacerations or episiotomies, endometritis, parametritis and thrombophlebitis, we get a corrected morbidity of 7.4 per cent (34 cases) in the nonprophylactic penicillin group, as compared to 2.2 per cent (10 cases) in the prophylactic group. This is well below the average quoted morbidity of (5 to 7 per cent) and represents an improvement of over 50 per cent in the corrected morbidity of this hospital.

Table II attempts to portray the difference in morbidity between early and late risers during both nonprophylactic penicillin months and prophylactic penicillin months. There is a definite improvement in both early and late risers using prophylactic penicillin noted particularly in the late risers, in whom we have 13 per cent morbidity in the nonpenicillin group compared with 4.5 per cent in the prophylactic group. The effect is not so noticeable in the early risers, in whom the comparison is 6.8 per cent to 4.9 per cent. It should be noted that, where penicillin is not used, early rising cuts this morbidity in half, but where prophylactic penicillin is used, the early rising appears to make no difference.

TABLE II. EFFECT OF EARLY AND LATE RISING ON MORBIDITY DURING PROPHYLACTIC AND NONPROPHYLACTIC PENICILLIN MONTHS

	NONPENICILLIN			PROPHYLACTIC PENICILLIN		
	NO. CASES	MORBIDITY		NO. CASES	MORBIDITY	
		CASES	PER CENT		CASES	PER CENT
Early rising	235	16	6.8	225	11	4.9
Late rising	222	29	13	221	10	4.5

In Table III, the percentage of morbidity is shown by months for both nonprophylactic penicillin and prophylactic penicillin groups. In general, it shows no regular seasonal variation for either group. All months except July, September, and November show an improved percentage morbidity using prophylactic penicillin.

TABLE III. SEASONAL VARIATION OF PERCENTAGE MORBIDITY (100.4° F.)

	APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	JAN.
Non penicillin months	8.5	9.4	19.5	3.4	10.8	4.2	14.7	4.2	17.6	16.6
Penicillin months	6.3	0	8	4.5	5.8	10	2.1	5.2	0	6

### Low-Grade Morbidity

It has been clearly shown that, when using the morbidity standard set by the American College of Surgeons, the use of prophylactic penicillin did reduce the maternal morbidity. However, as already stated, it is our intention to study further the maternal morbidity by selecting as a standard a temperature of 99.2° F. for over twelve hours excluding the first twenty-four hours. This low was selected for several reasons: (1) We believe that any rise of temperature above 99.2° F. should be considered a morbidity. (2) In many



pathologic conditions, the temperature never rises to 100.4° F., yet may be the basis for serious complications arising after the first ten days post partum, a pelvic cellulitis or mastitis for example. (3) Selecting this low standard makes the taking of temperatures every four hours necessary. This is not practiced in many maternity hospitals and we feel that the peaks of temperature often reached in the afternoon are being missed.

During the ten months in which prophylactic penicillin was given, 168 patients developed a temperature of 99.2° F. or over for more than twelve hours, giving a percentage morbidity of 37.6 per cent. Compare this with the preceding ten months in which no prophylactic penicillin was used and in which 252 patients developed a temperature of 99.2° F. or over, giving a morbidity of 54.9 per cent. An improvement of 17.3 per cent was noted with the use of prophylactic penicillin.

Table IV attempts to show the influence of prophylactic penicillin in reducing the morbidity during operative procedures. During the months in which no prophylactic penicillin was given, 81 patients were delivered by forceps operation, of whom 46 developed a temperature of 99.2° F., giving a percentage morbidity of 54.1 per cent, about the same as the general morbidity of this group. Low forceps of this group were associated with a slightly higher morbidity of 58.2 per cent. Compare this with the prophylactic group, in which 68 patients were delivered by low forceps, twenty of whom developed the low standard temperature, giving a percentage morbidity of 29.4 per cent, considerably less than the general morbidity of this group (37 per cent). This would tend to suggest that prophylactic penicillin does tend to reduce the morbidity associated with forceps deliveries.

TABLE IV. RELATION OF MORBIDITY (99.2° F.) TO OPERATIVE PROCEDURES

	NONPROPHYLACTIC PENICILLIN MONTHS			PROPHYLACTIC PENICILLIN MONTHS		
	TOTAL CASES	MORBIDITY		TOTAL CASES	MORBIDITY	
		CASES	PER CENT		CASES	PER CENT
Forceps	81	46	54.1	68	20	29.4
Midforceps	2	1	50	0	0	0
Low forceps	79	45	58.2	68	20	29.4
Versions and extractions	1	1	100	0	0	0
Perineal repair	162	89	54.9	173	53	30.6

One hundred sixty-two patients received some form of perineal repair during the control group of months, of whom 89 developed the low-grade temperature, giving a percentage morbidity of 54.9 per cent. Compare this to the prophylactic group in which 173 patients received some perineal repair, of whom 53 developed the above temperature, giving the percentage morbidity of 30.6 per cent—a considerable difference of 24.3 per cent.

There was only one case of version and extraction found in this series, so no comparison could be made there.

Table V gives a monthly comparison of percentage morbidity (99.2° F. or over for twelve hours). In general, it shows a considerable improvement during the months in which prophylactic penicillin was used as compared with corresponding months in which no prophylactic penicillin was used. No explanation could be found for the reverse in July and August.

TABLE V. SEASONAL VARIATION OF PERCENTAGE MORBIDITY (99.2° F. OR OVER)

	APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	JAN.
Nonprophylactic penicillin	51.3	52.8	63.9	32.7	41.3	55.9	67.6	57.4	69.3	53.5
Prophylactic penicillin	40.4	13.1	32.4	36.3	56.8	32.5	43.4	36.8	27.5	42.0

TABLE VI. EFFECT OF EARLY AND LATE RISING ON MORBIDITY (99.2° F.) DURING PROPHYLACTIC AND NONPROPHYLACTIC MONTHS

	NONPENICILLIN			PROPHYLACTIC PENICILLIN		
	MORBIDITY			MORBIDITY		
	NO. CASES	CASES	PER CENT	NO. CASES	CASES	PER CENT
Early rising	235	119	50.6	225	71	31.5
Late rising	222	133	59.9	221	97	43.8

TABLE VII. INCIDENCE AND PERCENTAGE OF CAUSES OF MORBIDITY (99.2° F.)

	SAPREMIA			MASTITIS			INFECTED EPISIOTOMY			PYELITIS			CHEST			PHLEBITIS			OTHERS			NIL NOTED		
	NO. CASES	PER CENT		NO. CASES	PER CENT		NO. CASES	PER CENT		NO. CASES	PER CENT		NO. CASES	PER CENT		NO. CASES	PER CENT		NO. CASES	PER CENT		NO. CASES	PER CENT	
Nonprophylactic penicillin	55	12		35	7.6		13	2.7		11	2.4		8	1.7		0	0		9	1.9		121	26.5	
Prophylactic penicillin	30	6.7		39	8.9		3	.6		9	1.9		3	.6		1	.2		4	.8		79	17.7	

TABLE VIII. AVERAGE DAYS IN HOSPITAL

	APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.	JAN.
Nonpenicillin months	10	10	10.4	9.8	10	9.6	10.2	9.8	10.8	9
Penicillin months	9.3	8.9	8.9	8.3	8	8.2	9.2	9.6	9.5	9.4

There appeared to be little seasonal variation, the highest percentage morbidity being in October and December. This agrees with the general opinion that in winter months when respiratory infections are more common, we can expect to have a somewhat higher morbidity. However, with the use of prophylactic penicillin, the only real variation was in August, at which time the temperature rose higher than any other month—for which no explanation is apparent.

Table VI compares the percentage morbidity of early and late risers during penicillin and nonpenicillin months. Early risers in the control group exhibit a 50.6 per cent morbidity, compared to 31.5 per cent under prophylactic penicillin, an improvement of 19.5 per cent. Late risers in the control group exhibit a 59.9 per cent morbidity, compared to 43.8 per cent morbidity under the prophylactic group—an improvement of 16.1 per cent.

In Table VII is shown the incidence and percentage morbidity of the various causes of the low-grade morbidity studied for both prophylactic and nonprophylactic groups. The greatest variation is seen in those conditions arising primarily from infection of the genital tract, i.e., as already noted, infected episiotomy or laceration, endometritis, parametritis, and thrombophlebitis.

Twelve per cent of the total patients of the control group became morbid due to sapremia, compared to 6.7 per cent during the prophylactic penicillin months. This represents a decrease of almost 50 per cent of cases developing the commonest form of genital infection (postpartum) by the use of prophylactic penicillin. This is statistically important.

Further, of the 55 patients of the control group who developed sapremia, 13, or 23.6 per cent went on to develop a temperature of 100.4° F. or over for more than twenty-four hours. Compare this with the prophylactic group where, of the 30 patients suffering from sapremia, 5, or only 16.6 per cent went on to develop a temperature of 100.4° F. or more for more than twenty-four hours. This may be significant although the number is not large enough.

During the control months, there were 162 perineal repairs, of which 13 became infected. Thus, 2.7 per cent of the control group developed a morbidity due to infected episiotomies. Compare this to the prophylactic group in which only 3 cases out of 173 with repairs developed an infection, representing 0.6 per cent of the entire group. This would seem to suggest that prophylactic penicillin has decreased the percentage morbidity due to infected episiotomies.

There was only one case of thrombophlebitis developing on the sixth day post partum. This patient was one of the late risers but had received prophylactic penicillin. No comparison is possible.

Prophylactic penicillin did not appear to have any appreciable effect on the incidence of breast infections. Out of 446 patients using prophylactic penicillin, 35 patients, or 7.6 per cent developed various degrees of mastitis. Compare this with 39 cases, or 8.9 per cent out of 457 cases not using prophylactic penicillin. The difference is not significant. However, 4 patients, or 10.2 per cent of the 35 cases, went on to develop a temperature of 100.4° F. for more than twenty-four hours. Compare this to the prophylactic group in which 2 patients, or 5.1 per cent of the 39 patients, developed this higher temperature. In neither group could we find evidence of abscess formation while in hospital.

As one would expect, there is no appreciable change in the incidence of pyelitis. Two and four-tenths per cent of the control group developed a morbidity due to pyelitis, as compared to 1.9 per cent of the prophylactic group.

Chest infections showed somewhat the same results—very little difference noted. Eight patients, or 1.7 per cent of the control group, developed a temperature due to chest infections compared with three patients, or 0.6 per cent of the prophylactic group. This is not significant.

Under the term "others" we listed all causes of morbidity not listed, such as finger infections, etc. "Nil noted" included those cases for which we could find no obvious cause for the temperature. Nothing statistically important could be drawn from either of these.

Table VIII gives the average hospital days per month of both groups. These represent the time from the day of delivery to day of discharge. It was impossible to exclude certain cases who were detained for various reasons not associated with morbidity, as awaiting transportation, severe toxemias, etc.

During the control months, the average hospital stay was 9.9 days compared to 8.8 for the prophylactic group, representing a hospital day saved for each patient. This in itself is statistically important.

In this series, there were no allergic reactions which could be attributed to the penicillin.

In a recent article in the *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY* (February, 1948), Pierce of Cincinnati produced somewhat the same results in reduction of morbidity using prophylactic penicillin in the form of vaginal suppositories.

### Summary

1. Four hundred forty-six patients received prophylactic penicillin intramuscularly every three hours for ten doses beginning immediately post partum, with a morbidity rate due to genital tract infection of 2.2 per cent using the "standard morbidity" and 37.6 per cent using the low standard selected (99.2° F. for more than twelve hours).

2. In the control group of four hundred fifty-seven cases, the morbidity rate was 7.4 per cent using the "standard morbidity" and 54.9 per cent using the low standard.

3. The effect of prophylactic penicillin associated with both early and late risers was compared with the nonprophylactic-penicillin group, using both the "standard morbidity" and the low standard of 99.2° F. An appreciable improvement in percentage morbidity was noted during use of prophylactic penicillin on both early and late risers.

4. The seasonal variation of morbidity for both groups using both standards of morbidity was noted. In general, it shows no regular variation. The monthly improvement of morbidity under prophylactic penicillin is noted.

5. The relation of operative procedures to morbidity was noted and the effect of prophylactic penicillin in reducing this morbidity studied. The percentage morbidity during operative procedures was definitely less with the use of prophylactic penicillin.

6. A study of the incidence and percentage of the causes of morbidity was made and the effect of prophylactic penicillin in reducing the incidence of these various diseases. The improvement was noted chiefly in those cases associated with genital tract infection. Fewer patients developing a temperature of 99.2° F. went on to higher temperatures.

7. Average hospital days per patient of both groups were compared.



## LEUCOPLAKIA OF CERVIX UTERI

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**L**EUCOPLAKIA of the cervix uteri is of practical importance for two reasons: (1) it may represent an area of noninvasive carcinomatoid changes, or (2) it may represent the first visible manifestation of an early established cancer. The problem of cervical leucoplakia and its conversion into established cancer is a vexatious one. The infrequency of the diagnosis of this condition in the cervix uteri has stimulated a review of the case records in the record department of the Elizabeth Steel Magee Hospital with some interesting findings.

Fourteen cases of leucoplakia of the cervix uteri were encountered from 1927 to 1946 in the Elizabeth Steel Magee Hospital. This number occurred in 103,685 gynecologic admissions. These fourteen cases were discovered among 8,906 patients having cauterization of the cervix and 1,221 of them who had tissue excised for biopsy purposes.

Résumés of the clinical records of these fourteen cases of leucoplakia follow. The first is that of Mrs. H. H., aged 43 years, a white woman who was admitted to the Elizabeth Steel Magee Hospital June 1, 1936, with a chief complaint of vaginal bleeding, loss of weight, fatigue and pain in the lower abdomen. Atypical vaginal bleeding had been present for ten months. The patient had had two miscarriages, one in 1918 and one in 1924, each approximately at two months, following a full-term pregnancy with a spontaneous delivery in 1919.

The examination was essentially negative except for the presence of a large fungating, extremely friable, freely bleeding growth involving the entire cervix. The uterus was not enlarged. On rectal examination there was some thickening of the base of the left broad ligament. The preoperative diagnosis was cancer of the cervix, but a frozen section of a biopsy specimen indicated it was nonmalignant. The permanent section showed dense, thick, stratified squamous epithelium which in areas was replaced by columnar epithelium. There were large prolongations of the stratified epithelium deep within the myocervium. These were composed of typical stratified squamous cells limited by a basement membrane and showing no invasive tendencies. Surrounding these areas of stratified squamous epithelium was a rather intense infiltration of round cells with a few eosinophiles and polymorphonuclear leucocytes.

On June 6, 1936, a diagnosis was made of leucoplakia of the cervix. Radium, 3,600 mg. hr., was applied to the cervical canal. The patient's course following radium was stormy. The result of the radiation therapy was satisfactory and the note in the clinic Oct. 20, 1936, indicated the cervix as roughened and nodular but freely movable. It bled readily. Cautery amputation of the cervix and other radium treatment were advised.

On Nov. 7, 1936, 3,000 mg. hr. of radium were applied to the cervix. On Nov. 13, 1936, a biopsy of the cervix was again made, a section of which showed microscopically islands of squamous epithelium growing in large sheets, invading the underlying tissue. The cells were large and pleomorphic and showed numbers of mitotic figures. The diagnosis was squamous-cell carcinoma of cervix (noncornifying type).

Radium, 2,400 mg. hr., was applied to the cervical canal April 16, 1937. A biopsy report at this time was not made.

Aug. 21, 1937, 2,400 mg. hr. of radium were applied to the cervical canal. At this time, there was an extensive malignant growth occupying the depth of the vagina. The cervical canal was represented by a craterlike opening surrounded by red, friable, easily bleeding tissue. The growth had extended into all contiguous pelvic structures. A biopsy was taken at this time. Following this last admission the patient was lost sight of.

The second case was Mrs. M. M., aged 65 years, a white woman who was admitted Aug. 11, 1936, with a chief complaint of whitish vaginal discharge and vaginal bleeding. These complaints had been present for a period of four months. The examination disclosed on the left portion of the cervix a whitish mossy-appearing growth slightly smaller than a dime. It bled easily on trauma. It was raised 1 mm. from the smooth surface of the cervix. There were some hardened points on the posterior vaginal wall. The preoperative diagnosis was leucoplakia of the cervix. The biopsy showed a growth of stratified squamous epithelium beneath which was a dense chronic inflammation. The growth rested on a dense fibromuscular stroma. There was an ulceration at one point. The epithelium grew in long sheets which extended into the underlying stroma. The nuclei of the cells were large and hyperchromatic. In one area there were isolated islands of cells which presented invasive tendencies. The diagnosis was leucoplakia of the cervix with beginning malignant changes.

Radium, 1,900 mg. hr., was applied to the cervical canal following cautery resection of the cervical growth on Aug. 12, 1936. This patient had Parkinson's disease and pronounced arteriosclerosis.

On Feb. 2, 1937, the cervix was adherent to the posterior vaginal wall by light adhesions which were separated. There was some redness around the os with leucoplakia present in this area and also in the posterior vaginal wall. The cervical canal was readily dilated.

A biopsy was done Feb. 5, 1937, which showed intense scarring of the cervix. No tumor cells were seen.

On Feb. 5, 1937, 2,500 mg. hr. of radium were applied in the cervical canal.

The patient continued to have bleeding from the cervix and vaginal tissue with a considerable purulent discharge from the uterus and cervix. The appearance grossly was that of malignancy.

On July 27, 1937, there was induration extending outward into each broad ligament. It was diagnosed as Class IV carcinoma. On July 30, 1937, radium (2,400 mg. hr.) was again applied.

The patient was seen March 8, 1938, and no evidence of residual malignancy was found.

The third case is that of Mrs. P. C., aged 36 years, a white woman who was admitted with a history of metrorrhagia and leucorrhea for which she had a cauterization of the cervix March 27, 1939. No biopsy was taken. The preoperative diagnosis was chronic cervicitis with erosion and leucoplakia of the cervix uteri.

The clinical course following this procedure was satisfactory without the development of malignancy.

The fourth case was that of Mrs. W. S., aged 39 years, a white woman who was admitted Oct. 22, 1939, with complaints of meno-metrorrhagia, vaginal discharge, and lower left quadrant abdominal pain. All of these symptoms were of approximately five months' duration. There had been two full term pregnancies and no miscarriages. Her menopause was at age 34 years following a surgical operation. The cervix was enlarged, bilaterally lacerated, and showed Nabothian cysts as well as an area of erosion. There also was a grayish-white area of leucoplakia near the right end of the tear. The cervix was covered with purulent exudate. The uterus, tubes, and ovaries were essentially negative, excepting for an enlarged, cystic, tender left ovary. The patient was discharged without operation. No follow-up could be obtained.

The fifth case was that of Mrs. M. S., aged 61 years, a white woman who was admitted with a history of vaginal bleeding over a period of twenty months without having had a pelvic examination. She had had three pregnancies, two of which were full term and one a miscarriage at five months.

The examination disclosed the cervix to be three times normal size. The right side of the cervix was occupied by a granular, friable, freely bleeding, somewhat irregular mass with a narrow rim of normal-appearing cervical tissue surrounding it. There was induration of the base of each broad ligament, more marked on the left side. The uterus was enlarged to two and one-half times its normal size. The adnexa were not palpable.

Histologic diagnosis on Sept. 12, 1936, was leucoplakia with early malignant degeneration. The section was covered by stratified squamous epithelium which was quite thick with broad epithelial pegs. The epithelium had broken through the basement membrane and was extending into the underlying tissue in many places.

A second biopsy on Sept. 26, 1936, showed the same type of reaction. There were applied to the cervix 2,400 mg. hr. of radium from Sept. 26 to Sept. 28, 1936. From Oct. 2 to Oct. 4, 1936, 2,400 mg. hr. of radium were applied to the cervix. Excessive bleeding from the cervix followed this treatment. She had a repair of an incarcerated hernia on Jan. 7, 1937.

The next admission was April 13, 1940, with a history of having had constant bleeding for four months. She was suffering from a severe secondary anemia. The examination at the time of this admission revealed a plaque of apparent carcinomatous tissue in the upper vagina near the site of the cervix. The growth extended along the anterior vaginal wall into the bladder and through the pelvis forming a characteristic frozen type of pelvis. A biopsy was performed on April 16, 1940, which was reported squamous-cell carcinoma of the cervix. The section revealed irregular sheets of squamous epithelial cells growing in all directions. Mitotic figures were numerous. Small early pearl-like formations were present (atypical cornifying type). She received 600 r. onto the cervical site through the intracavitary cone and 2,400 r. externally over the pelvis.

The patient was discharged to her home and her condition was improved when last heard from in November, 1940.

The sixth case was that of Mrs. V. P., aged 40 years, a white woman who was admitted June 18, 1941, with a history of right-sided pelvic pain and urinary incontinence.

The examination disclosed an enlarged, cystic, bilacerated cervix with two small areas of leucoplakia which showed a positive Schiller test. The uterus was enlarged and there was some thickening of the parametrium. On June 23, 1931, the patient had a dilatation and cauterization of the cervix and Sturmdorf amputation with a Manchester anterior colporrhaphy and perineorrhaphy. The microscopic diagnosis from cervical tissue was active metaplasia of cervix, chronic endocervicitis with Nabothian cysts. The patient when last seen in the dispensary Aug. 28, 1941, was in good health.

The seventh patient was Mrs. M. A., aged 45 years, a white woman who was admitted May 21, 1942, with a complaint of pain in the lower abdomen and menorrhagia. The latter complaint had been present for the previous sixteen months. Her mother and sister had had cancer of the breast. The patient's breasts were negative. There was a firm movable mass in the pelvis reaching to three fingerbreaths below the umbilicus. The cervix uteri was lacerated, cystic, and showed the scars of two previous office cauterizations. On the left side of the angle of the cervix was an enlarged patch of white epithelium extending from the os to the periphery of the cervix. This could not be scraped off readily. It was diagnosed as metaplasia or leucoplakia. Preoperative diagnosis on May 22, 1942, was chronic cystic cervicitis, questionable leucoplakia of cervix, leiomyomas of the uterus, and endometriosis of left ovary. The operation was biopsy of cervix, cautery amputation of cervix, supravaginal hysterectomy, and left salpingo-oophorectomy. A microscopic section of the cervix showed in one area the squamous epithelium to be moderately thickened, sending long pegs of epithelium into the underlying tissue. The patient was free of evidence of pelvic disease on Nov. 16, 1944. A cystoscopic examination at this time was negative.

The eighth patient was Mrs. S. W., aged 44 years, a white woman who was admitted June 29, 1942, with a chief complaint of backache and leucorrhea which had been present for a period of one and one-half years. The examination disclosed a cervix moderately enlarged, bilacerated, and which contained several white, raised areas which did not stain when Churchill's iodine was applied.

The pre-operative diagnosis was cystocele, rectocele, and leucoplakia of the cervix. On July 1, 1942, an anterior colporrhaphy, Hegar perineorrhaphy, hemorrhoidectomy, total hysterectomy, and appendectomy were performed. The pathologic diagnosis on July 1, 1942, was chronic endocervicitis with Nabothian cysts, leucoplakia of cervix, endometrium—late lutein phase, mild chronic metritis, chronic interstitial appendicitis. Histologic sections of cervix were partially covered by keratinized columnar and stratified squamous epithelium. At the region of the pale white plaque noted grossly, the stratified squamous epithelium sent a few short narrow pegs toward the deeper tissues. There was also a low-grade chronic inflammatory reaction associated with the above.

The ninth case was Mrs. E. M., aged 62 years, a white woman who was admitted with chief complaints of incontinence of urine and prolapse of the pelvic organs. These complaints were of six months' duration. There was relaxation of the perineum and a cystocele with a second-degree prolapse of a small uterus. The cervix was hypertrophied with a clean external surface. The operation on Oct. 16, 1942, was a Manchester anterior colporrhaphy, repair of enterocele, amputation of the cervix, and a Hegar perineorrhaphy. The pathologic diagnosis was chronic endocervicitis and early leucoplakia with keratinization. Histologically, the section was composed of stratified squamous epithelium which in one place was very thick and covered on the surface by keratin. A low-grade chronic inflammation was associated. The patient when last seen on Dec. 8, 1942, was free of complaints.

The tenth patient was Mrs. M. D., aged 29 years, a white woman who was admitted June 28, 1942, with a history of pain in the lower abdomen and back of five months' duration. The clinical diagnosis was chronic cervicitis. The operation on June 30, 1942, was biopsy of the cervix and cauterization of the cervix. The laboratory diagnosis was leucoplakia of cervix uteri. Histologic sections of cervix showed a surface covered with a heavy layer of keratinized stratified squamous epithelium. The epithelium showed papillary infoldings. There was an associated chronic inflammatory reaction.

A second admission on Feb. 11, 1945, because of leucorrhea of six months' duration resulted in a clinical diagnosis of leucoplakia of the cervix and postcauterization stenosis of the cervix. On Feb. 13, 1945, a biopsy of the cervix, cauterization of the cervix, and insertion of stem pessary were performed. Histologically, a section of the cervix again showed surface epithelium thick and heavily keratinized. The pathologic diagnosis was chronic endocervicitis. The patient's condition was satisfactory when last seen.

The eleventh patient was Mrs. A. S., aged 42 years, a white woman who was admitted Sept. 27, 1943, complaining of a low back pain of five years' duration. An examination disclosed a complete prolapse of the uterus associated with a cystocele, rectocele, and relaxation of the perineum. The cervix was lacerated and presented a zone of erosion about the external os. The uterus was small. The patient had an anterior colporrhaphy (Manchester type); a Sturmdorf amputation of the cervix, and an Emmet perineorrhaphy on Sept. 29, 1943. The laboratory diagnosis was leucoplakia of the cervix with metaplasia. Histologic section showed the surface epithelium to be thick and covered with keratin. It showed beginning proliferation of the deep layers at the external os where active metaplasia was seen. A low-grade chronic inflammation was present. When last seen April 3, 1944, the patient's condition was satisfactory.

The twelfth case is that of Mrs. E. D., aged 71 years, a white woman who was admitted July 15, 1945, with a chief complaint of protrusion of the pelvic organs from the vagina. An examination disclosed a third degree prolapse of the uterus and a relaxed and lacerated perineum with rectocele. The patient had had on Aug. 8, 1944, a Watkins Interposition operation, an amputation of the cervix, and a Hegar perineorrhaphy. The pathologic



diagnosis on the portion of the cervix submitted was leucoplakia of cervix with mild keratinization and chronic cervicitis with ulceration. The histologic picture revealed the continuity of the stratified squamous epithelium to be interrupted by areas of ulceration containing necrotic tissue, hemorrhage, and polymorphonuclear leucocytes. The stratified squamous epithelium was thickened and keratinized. Lymphocytes had infiltrated the wall. In October, 1944, there developed an enterocele which was repaired Oct. 31, 1944. The patient has remained well to date.

The thirteenth patient is Mrs. E. W., aged 38 years, a white woman who was admitted Feb. 18, 1944, with a chief complaint of pain in the right lower abdominal quadrant and dysentery. The physical examination was essentially negative. It is noted that the cervix was nulliparous in type and presented a small white area adjacent to the os which did not rub off. The uterus was retroverted and fixed. The adnexa were tender and there were very tender nodules in the cul-de-sac. The findings were suggestive of endometriosis. The patient ran a moderate temperature. She had a leucocytosis and a rapid sedimentation rate. On March 15, 1944, with a preoperative diagnosis of chronic cervicitis (possible thrush infection), bilateral subacute salpingitis, and cystic left ovary, the following operation was performed: biopsy and cauterization of the cervix, bilateral salpingectomy, left oophorectomy and supra-cervical hysterectomy. At the time of operation, the above-mentioned whitish plaque in the surface of the cervix was considered to be due to a Monilia infection. A biopsy was taken from this point, a report from which is included in the following. At the time of operation both tubes were enlarged and surrounded by dense fibrous adhesions. The ovaries were cystic. The pathologic report was endometrium-follicular phase, chronic perimetritis, leucoplakia of cervix uteri with beginning surface carcinoma, marked chronic salpingitis and perisalpingitis, cystic follicles of ovary with chronic perioophoritis. The histology of the cervical biopsy showed thick keratinized surface epithelium with the cells in the thicker portions showing metaplastic changes. In the metaplastic areas the epithelial cells had taken on distinct pleomorphic changes, presenting a typical picture of a leucoplakia of the cervix with beginning surface carcinoma. No further treatment was given this patient and when last seen her condition was satisfactory.

The fourteenth patient was Mrs. M. B., aged 52 years, a white woman who was admitted March 26, 1945, with a chief complaint of a bloody vaginal discharge, which had been preceded by a period of amenorrhea of approximately eight months' duration. The examination was essentially negative, except for the presence of a cystic cervix containing a polypoid mass. This mass completely filled the cervical os. A cholecystogram, March 30, 1945, disclosed the presence of gallstones with a preoperative diagnosis of a cervical cyst and cholelithiasis. The following operation was performed: dilatation and curettage, removal of cervical cyst, cauterization of cervix, and cholecystectomy. The laboratory diagnosis on April 1, 1945, was endometrium-senile type, chronic endocervicitis with Nabothian cysts and beginning leucoplakia, and chronic cholecystitis with cholelithiasis. The cervix histologically showed surface epithelium which was thick in places and beneath which were areas of dense chronic inflammation. The patient at the time of last examination was in good condition.

### Summary

Fig. 1 demonstrates a leucoplakia of the cervix uteri and presents a rather sharp contrast in the cellular architectural pattern to that shown in Fig. 2. The latter demonstrates a typical noncornifying squamous-cell carcinoma of the cervix uteri. The thick keratinized epithelium referred to many times in this report, together with an area of superficial ulceration and "rete peg" formation are shown in Fig. 1. For many years speculation concerning the relationship of leucoplakial epithelial thickening to subsequent malignant changes has existed. This relationship has not yet been proved, but in many cases certainly seems to exist.

In 103,685 gynecologic admissions, there were 14 cases diagnosed as leucoplakia of the cervix uteri. It is worthy of note that four (28.5 per

cent) out of these fourteen patients diagnosed as having leucoplakia of the cervix uteri developed carcinoma of the cervix at a future time. Two of these four patients having carcinoma of the cervix had this condition at the time of first biopsy. The series of cases given is small and consequently no positive accurate conclusions can be drawn. However, from following patients having such lesions, it is our impression that a very definite relationship exists between leucoplakia of the cervix and subsequent malignant growth.



Fig. 1.

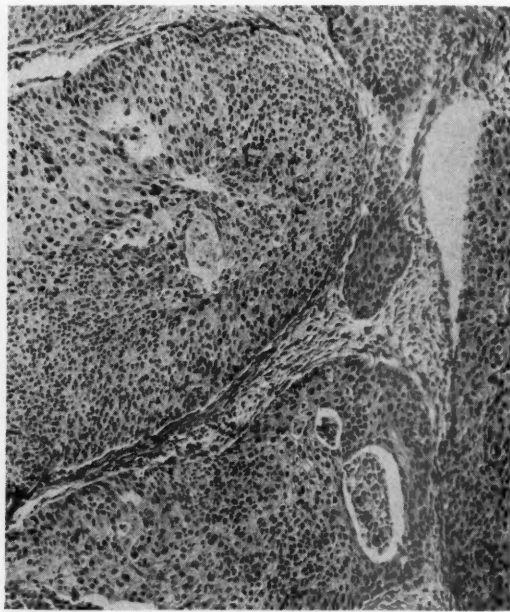


Fig. 2.

Fig. 1.—Leucoplakia of the cervix showing thickening of the epithelium with rete peg formation and superficial areas of ulceration. Chronic inflammatory cells are seen beneath the epithelium. Very little keratin is present on the surface.

Fig. 2.—Noncornifying squamous-cell carcinoma of the cervix with typical epithelial-cell architectural pattern in contrast to section shown in Fig. 1.

### Conclusions

1. A pale or white, slightly raised, discrete, circumscribed area, appearing on a background of pale pink cervical mucosa should be regarded with suspicion. These areas can readily be detected with a naked eye, rendering the use of a colposcope unnecessary. All such areas should be biopsied.

2. A leucoplakic lesion of the cervix is potentially malignant and should be regarded and treated as such.

3. A blanched, thickened area of epithelium on the cervix is more significant in a patient during the reproductive period of life than following the menopause.

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## THE USE OF THE MALE LEOPARD FROG (*RANA PIPIENS*) AS A PREGNANCY TEST ANIMAL\*

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EARLY in 1948, Wiltberger and Miller<sup>7</sup> briefly reported the use of the male frog *Rana pipiens* in a test for pregnancy. They reported no false negatives in the first trimester of pregnancy, and no false positives when using the urine from nonpregnant women and from men. Two hundred animals were used in the tests. As the technique described was simple, the test animal easy to obtain and relatively inexpensive, and the reported results extraordinarily accurate, it was decided to put the method to clinical test.

Between March 3 and August 31, slightly over 100 urines from patients were examined. During the progress of this work, the paper of Robbins and Parker<sup>5</sup> appeared, reporting essentially the same results, using essentially the same technique as that described by Wiltberger and Miller. In 122 urines examined, they reported one false negative in 78 known pregnancies. Ten normal, menstruating controls and 34 cases of amenorrhea, negative by Friedman or Aschheim-Zondek tests, were all frog negative. Galli-Mainini and others<sup>1, 2, 4</sup> have similarly used South American male toads.

### Technique

As originally described, 5 c.c. of untreated morning urine were injected into the dorsal or lateral lymph sacs of two or more male frogs (*Rana pipiens*). The frogs were placed in separate glass jars, and, two to four hours later, the accumulated urine was examined microscopically for the presence of spermatozoa. The test animals were reused in four or five days. Robbins and Parker used essentially the same technique, except that they filtered the urine, and took cloacal smears, beginning one hour after injection. They reported some of the urines toxic and killing the frogs before a positive reaction could be obtained. To obviate this, they suggested injecting the urine in divided dosage.

At the beginning, I followed the technique as outlined by Wiltberger and Miller, but very soon was discouraged by the number of animals killed by the injections. As it appeared that the volume of fluid injected might be a factor in the death of animals, it was decided to try a concentration-detoxification method. This has proved most successful.

The technique used is as follows: 100 c.c. (if somewhat less is available, it is diluted to 100 c.c. with water) of morning urine is placed in a stoppered graduate, adjusted to pH 4 with 20 per cent hydrochloric acid, 5 c.c. of a hydrous aluminum silicate adsorbent† added, and the mixture well shaken by hand. It is allowed to stand for ten minutes, the supernatant fluid is discarded, and the remainder transferred to a centrifuge tube and centrifuged for about three

\*Part of the cost of animals was defrayed by a grant from the Gynecology Department Research Fund.

†"Adsormone," purchased from Louis C. Herring & Co., Orlando, Florida. Detailed directions for its use accompany the material.



minutes. The supernatant fluid is discarded; the precipitate is ground up with five to ten c.c of N/10 sodium hydroxide. The mixture is centrifuged, and the supernatant fluid is poured into a test tube where it is neutralized with 20 per cent hydrochloric acid, using phenolphthalein as an indicator. 2.5 c.c. of this is then injected into the dorsal lymph sac of a male frog. The preparation of the concentrate takes less than one-half hour. The frogs were, at first, kept in individual covered glass dishes. More recently they are kept in covered glass funnels, having a diameter of five to six inches. In this way, the urine is collected in beakers, and it is very simple to catch a recently passed drop of urine from the funnel tip. If none has been passed, disturbing the animal, or gentle handling, usually produces urination. The urine is examined approximately every hour for four hours, or less if an earlier positive is obtained. Positive tests were occasionally obtained as early as forty minutes after injection, though no effort was made to find out how early spermatozoa might appear in the urine. Contrary to the experience of Robbins and Parker, in a few instances, urine which contained no spermatozoa at two hours were positive at four. While in most positive cases, the numbers of spermatozoa found were large, and frequently in aggregations as pictured by Robbins and Parker, there were a number of cases, particularly in very early pregnancies, where the numbers were very small, and the drops of urine had to be carefully searched under the microscope. The necessity for using more than one frog, as suggested by both groups of previous investigators, is confirmed; occasional frogs which did not react were encountered, and quantitative differences in reactivity were frequently noted.

Both previous reports stressed the fact that information was lacking about any possible seasonal variation in response to pregnancy urine. Both reports had dealt with winter frogs. Robbins and Parker speculated if special precautions might have to be taken during the breeding season. Glass and Rugh<sup>3</sup> have described for *Rana pipiens* a single annual maturation cycle for spermatozoa, starting after the breeding season and completed in November. The mature spermatozoa are stored in the seminiferous tubules until release during the breeding season. Rugh<sup>6</sup> has expressed doubt that sufficient numbers of spermatozoa were available for release during the summer months to permit the use of the male *Rana pipiens* as a pregnancy test animal. However, their illustrations indicate that spermatozoa are present in the seminiferous tubules during the summer months; the results hereinafter described indicate that they are released under gonadotropic stimulation. The first two reports dealt with results with winter frogs, when large numbers of stored spermatozoa are ready for release. The tests herein reported were run during the spring and summer. The impression has been obtained that in August the frogs emitted smaller numbers of spermatozoa following injection of pregnancy urine. Almost never in August were aggregated numbers of spermatozoa, as pictured by Robbins and Parker, seen, and as had been so frequently seen in earlier months.

One unexpected source of error was encountered during the progress of the investigation. The work was started during the breeding season when the sexual differences of the frogs were striking. As summer approached, the dimorphism became less striking, and in some individuals it was difficult to be certain of the sex; in some instances errors were made. The male is characterized by thicker, pigmented thumbs, and the presence of air sacs, which usually inflate during croaking. To obviate this difficulty, as well as for the reasons cited by Robbins and Parker, the frogs were sacrificed at the end of a test, and their gonads were examined. (Probably with greater experience, the error of sexual differentiation will become very low. Male frogs were ordered from the dealers; one of the two dealers with whom I have had experience has been much more successful in sending a very high percentage of male animals.)



### Results

One hundred-fourteen specimens of urine (from 104 individuals, including one male suspected of having a testicular tumor) were examined. Fifty-five positive frog tests were obtained, which were confirmed either by a Friedman test or by clinical signs of pregnancy. Positive tests were obtained as early as, in one case, the thirty-fourth day, in another, the thirty-seventh day of a cycle. In the former, a concomitantly performed rabbit test was negative; the frog test was very weakly positive; only rare spermatozoa were found in the urine of one of the two frogs injected. The woman is clinically pregnant. In the latter, artificial insemination had been performed on the fifteenth day, counting from the first day of the last menstrual period. In one case a negative test was obtained on the 32nd day, and a positive one 21 days later. Contrary to the experience of Wiltberger and Miller, positive tests were obtained from women on the delivery table—catheterized specimens removed immediately prepartum. In two instances, positive tests were obtained 3 and 6 days after passage of hydatidiform moles.

Forty-eight negative frog tests were confirmed either by Friedman test, by surgical operation (laparotomy, hysterectomy, or curettage) or by subsequent clinical course. Included is one case, with last menstrual period fifteen days before, suspected of being an ectopic pregnancy, in which both frog and rabbit tests were negative. Curettage showed a late proliferative phase, but with a single focus showing decidua. A second frog test twenty-four days later was again negative; the patient was still amenorrheic, but there were no clinical signs of pregnancy, and this was confirmed by the subsequent clinical course. One case perhaps deserves special comment. On July 16, the frog test was negative, whereas the rabbit test gave a questionable positive reaction. On the morning of July 20, the frog test was repeated and was again negative. A hysterectomy performed that afternoon showed no evidence of pregnancy.

There remain to be discussed eleven false negative tests. Three of these represent pregnancies, probably too early to give a positive reaction. One was a young woman whose last menstrual period was on March 28; the frog test was negative on April 29; a repeat on May 20 was positive. The second case was in a 40-year-old woman with a very irregular menstrual history. Her last menstrual period was said to have been on March 23. A frog test on July 16 was negative; a simultaneously performed rabbit test was probably positive. A rabbit test said to have been performed one week before, had been reported as negative. A repeat frog test ten days later was positive. The third case was that of a woman whose last menstrual period had been on June 25; the negative frog test was made on August 4, at which time the Friedman test was positive. A repeat frog test with urine collected on August 9 gave a weak positive reaction. Spermatozoa were found only in a single sample of urine, entrapped in a bit of mucus.

One case occurred in a young woman who brought her first urine three days after she missed her first period. She had a regular twenty-eight day cycle. Four days later, and seventeen days after that, repeat frog tests were run, which both were again negative. A rabbit test performed at the time of the last test was positive. Four days later another frog test was negative; two days later a spontaneous abortion occurred.

There were two cases of negative frog test with positive rabbit test in which abortion occurred. One of these was a tubal abortion in which practically all the chorionic tissue had been destroyed by hemorrhage. Operation was done two days after the frog test. The abortion consisted of mostly necrotic placental tissue.

In one patient with last menstrual period on May 28, on whom a positive frog test was confirmed by a positive rabbit test, performed on August 3, a repeat was done on August 9

because the patient had begun to bleed. At this time, the frog test was negative. A rabbit test was not done. The patient subsequently aborted. Probably this should not be classified as a false negative. Placental death may have occurred previous to the second test. One patient on whom the frog test was negative and the rabbit weakly positive, on several occasions passed some decidual tissue, subsequently this patient aborted.

### Discussion

The results herein reported confirm in essential details those previously reported with the male frog. There have been no false positive tests. A number of false negative tests were obtained, more than had been previously reported using either the male frog<sup>5, 7</sup> or male toad.<sup>1, 2</sup> However, the method was here put to more severe test inasmuch as the routine cases of hospital and office practice were utilized, and the more difficult clinical problems subjected to study. Examination of the false negatives show that all but two of them occurred after the last week in June. The two early ones were a missed abortion in which the rabbit test was only weakly positive; and one very early pregnancy, in which a parallel rabbit test was not performed. It might well be that the false negative reactions in the later cases are due to the lesser reactivity of the frog during the early phase of the maturation cycle, when numbers of stored spermatozoa are presumably few. The observations of Glass and Rugh are based on very few animals at each month of the cycle, and little information is available on the extent of individual variations. There have been numbers of instances, in confirmed positive cases, in which only one of the two frogs injected emitted spermatozoa under the stimulus of pregnancy urine. Further experience might teach that during the summer months, perhaps June through September, more than two frogs should be injected, and perhaps also a more concentrated urine extract should be used.

In spite of theoretical objections that the test would not work during summer months,<sup>5</sup> it has proved most useful. It has been utilized as a guide in the handling of several cases of suspected ectopic pregnancy, in which the rapidity with which an answer could be obtained was of clinical importance. In several instances, a test run in the forenoon gave an answer before an operation scheduled tentatively for early afternoon. I can confirm, from the experiences of several of our obstetricians and gynecologists, the prediction made by Robbins and Parker that "the rapidity that it affords makes of the test an emergency procedure of possible benefit in difficult diagnostic problems."

The test is simple and inexpensive. The preparation of the urine and the injection of the frogs can be done by the average well-trained technician. Spermatozoa, when they are numerous, are unmistakable. When they are few, more experience is necessary for their recognition. Frogs are cheap, and the use of Adsormone adds little to the cost of the test. No special laboratory equipment is required. The frogs are stored in wire-mesh-covered five-gallon discarded metal drums, and kept in or over a sink. Water trickles through, and escapes from holes punched in bottom and sides. Frogs, as a rule, are kept for a week or less. During the summer months, if they are kept longer, "red-leg" becomes a problem. The differentiation of sex, although in some animals difficult, is not too serious a difficulty if each frog is checked by dissection after the test is completed. When one frog is negative, and the other a female, the test can be repeated very quickly. When frogs are certainly male (inflated air sacs), it is possible to utilize them again, as was done by Wiltberger and Miller. On several occasions, following a negative test, the same frogs were injected one to three days later with urine from known pregnancies, and positive tests were obtained. I feel, however, as stated above, that it is better to use frogs only once, and to sacrifice them after each test.

It has not been determined as yet if the test can be used for quantitative determination of gonadotropin. It may well be that the cyclic change in the seminiferous tubules introduces a variable which would make quantitative results not possible, except perhaps in the winter months.

### Summary

The successful use of the male common leopard frog, *Rana pipiens*, in a test for pregnancy, as described by Wiltberger and Miller, and Robbins and Parker, is confirmed.

A modification of the method is described. This modification eliminates the killing of numerous frogs by "toxic" urines, which was early found a serious drawback to the performance of the test as originally described.

The test is reliable (no false positives), although some false negatives were found. The test may be used in summer as well as winter months, though it may prove necessary to use more frogs for each test in the summer, to allow for individual variation in reactivity.

The test is inexpensive, and is sufficiently rapid to be of great value in clinical emergencies, as originally predicted by Robbins and Parker.

It is sufficiently simple so that it may be used even in the smallest laboratories without special equipment, or provision for care of animals.

Acknowledgments: Mr. Saul Saffer gave much help in the preparation of urines and the handling of the animals. I want to thank the several obstetricians and gynecologists who supplied urines from their private practices.

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## TOLERANCE TRIAL OF NEOSTIGMINE METHYLSULFATE IN PREGNANCY

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CONSIDERABLE controversy exists regarding the possible dangers arising from the use of neostigmine in the pregnant surgical patient and for the diagnosis of pregnancy. The present study was undertaken for the following purposes: (1) to determine whether neostigmine methylsulfate\* has any effect on the course of pregnancy when administered to gravid women at various stages of gestation; and (2) whether the drug exerts any deleterious effect when used early in pregnancy as a diagnostic aid.

### Method

Four groups of patients were picked at random from the clinic of the Boston Lying-in Hospital. The first group, numbering twenty cases, was composed of women in the seventh through the fourteenth week of pregnancy. These patients received 2 c.c. of 1:2,000 neostigmine methylsulfate intramuscularly for three successive days. This is the dosage schedule as outlined for the pregnancy test.<sup>1</sup> The first injection was given as the patient was visiting the prenatal clinic, and the second and third injections were administered at home.

The second, third, and fourth groups were composed of ten patients in the fourteenth through twenty-seventh week, twenty in the twenty-eighth through thirty-fifth week, and twenty in the thirty-sixth week through delivery. The latter three groups were not necessarily normal gravid patients, since their availability as subjects was because they had been admitted to the hospital for various medical conditions. The only patients specifically excluded in this study were those showing signs of vaginal bleeding where there was a possibility of threatened abortion, premature separation of the normally implanted placenta, or placenta previa. The majority of these patients in the latter three groups received 1 c.c. of 1:2,000 neostigmine methylsulfate intramuscularly at intervals of three hours for six successive doses, constituting a total of 3 mg. in fifteen hours.

The first group of twenty cases had seven patients who showed no subjective symptoms or objective signs following neostigmine on three successive days. Seven patients experienced minimal subjective symptoms after either their first or second dose. None had any objective signs, i.e., change in blood pressure or pulse rate. Subjective symptoms included slight dizziness, headache, nausea and vomiting, salivation, and diarrhea. Following each of the two injections, four patients showed the same symptoms of slightly greater intensity. Thick tongue and difficulty of speech of a transient nature were noted in two cases.

One patient, who had diabetes mellitus, complained of slight gagging sensation after the second injection, and flatulence following the third. Another patient received two injections following which she began to bleed.

\*Neostigmine methylsulfate used in this study was supplied by Hoffman-LaRoche, Inc.



The biological test for pregnancy was positive. She was admitted to the hospital where a vaginal examination under ether anesthesia indicated a normal pregnancy. There was no apparent cause for bleeding. On questioning, it was learned that three weeks previously she had received three daily injections from her family doctor which had resulted in vaginal bleeding on the fourth day. Her pregnancy continued and she was delivered normally at term. Fifteen patients of this group have been delivered of sixteen infants who are living and well. Five patients are still undelivered with apparently normal pregnancies.

The second group of ten cases had eight patients who showed no subjective symptoms or objective signs. One patient experienced nausea and vomiting and headache following the first or second injection, and a second had an exacerbation of an existing headache after three injections. Three patients of this group have been delivered. Two of the infants are living and well. The third was a sensitized Rh-negative patient. She was delivered of a stillborn fetus, death being due to erythroblastosis of the hydrops type. Two patients have undergone therapeutic abortion. Five are undelivered, three of these pregnancies being complicated by hypertension and albuminuria of a mild character.

The third group of twenty cases had twelve patients who had no subjective symptoms or objective signs. Seven patients had symptoms of varying intensity such as nausea, headache, warm flushing, dizziness, frequency, abdominal cramps and gas. None of these symptoms were of any magnitude, the most prolonged being thirty minutes while the majority were more transitory. In one of the three patients complaining of abdominal cramps there was the possibility that these were uterine in origin. One patient had no symptoms, but stained a minute quantity of blood on voiding after the third injection. None had any objective signs. Fifteen patients in this group had been delivered of twelve infants who are living and well. Two infants died, one of marked prematurity. The other died of atelectasis for no apparent cause. There was one stillbirth resulting from toxic separation of the placenta which occurred eight days following the neostigmine tolerance test. Five patients are undelivered.

In the fourth group of twenty cases, twelve patients showed no symptoms. Two of this group had objective signs with one showing slight staining following her third injection, and one patient with ruptured membranes but no labor, showing a rise in blood pressure following the first three injections. Three patients who were at term went into labor during the course of injections. Minimal signs were experienced in four cases, and one patient was uncooperative necessitating withdrawal of the drug after four injections. Twenty women have been delivered with nineteen infants living and well. There were two stillbirths, one a twin from a sensitized Rh negative mother, the other from a mother with severe pre-eclampsia. All of these patients in this group represented either major or minor obstetric problems.

### Summary

Seventy patients in various stages of pregnancy ranging from the seventh week through delivery received intramuscular injections of neostigmine methylsulfate. Twenty patients in the first trimester received 2 c.c. of 1:2,000 on three successive days. There was no interference with normal gestation, and fifteen patients have been delivered of sixteen infants who are living and well. The five patients remaining undelivered are following normal prenatal courses.

Fifty patients from the fourteenth week through delivery received 1 c.c. of 1:2,000 neostigmine methylsulfate every three hours for six doses. The drug

did not produce any noteworthy subjective symptoms or objective signs of an alarming nature. Forty patients have been delivered of thirty-three infants who are living and well. Two infants died following delivery. There were four stillbirths, one a twin. Two patients underwent therapeutic abortion. Ten patients remain undelivered.

### Conclusions

(1) Neostigmine methylsulfate can be safely used in the nonbleeding pregnant patient. (2) When used in early pregnancy as a diagnostic aid, the drug does not interfere with normal gestation, but produced distressing signs in one patient.

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## **HYPEREMESIS GRAVIDARUM WITH RETINAL HEMORRHAGE\***

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THE standard textbooks and medical literature exhibit a paucity of information regarding hemorrhagic retinitis in severe vomiting of pregnancy. It is the purpose of this paper to add one typical case to the literature and to emphasize that the high mortality associated with this condition can be lowered only by earlier recognition and proper treatment. Moreover, it may serve to stress further Stander's plea for routine examination of the eyegrounds in the early, as well as the late, toxemias of pregnancy.

Since the first reported case by Erisman in 1890, Stander, Ballantyne, and others have brought the total reported cases to eleven, of which eight were fatal. This case brings the total to twelve, with a mortality of seventy-five per cent.

### **Etiology**

The consensus of opinion is that a disturbance in the metabolism of the carbohydrate chain leads to dehydration, starvation, and incomplete oxidation of fatty acids. This may be a productive factor in the disease, but it is not clear what etiologic agent initiates the vomiting. More recently, Smith and Smith have clearly demonstrated the presence of a toxin, euglobulin, in patients suffering from pre-eclampsia and eclampsia. Perhaps further research will reveal a similar or identical toxin inherent to the pathogenesis of early, as well as late, toxemia of pregnancy. Such a toxin is a plausible explanation for the pathology and response to termination of the pregnancy.

### **Symptoms, Signs**

The usual progression of events in severe vomiting of pregnancy is vomiting, weight loss, dehydration, blurring of vision, hemorrhages into the retina, sometimes generalized petechial hemorrhages, and death.

The abnormal chemical changes in the blood and urine of these patients are reflections of dehydration, starvation, incomplete oxidation of fatty acids, and tissue destruction. Dieckmann and Crossen report no marked urine changes except decreased chlorides and increased ammonia nitrogen. Peckman, Dieckmann, Crossen, and Schjott-Rivers report the blood changes as a definite increase in nonprotein nitrogen, uric acid, and urea, a decrease in chlorides and little change in the carbon dioxide combining power. The blood sugar does not seem to be greatly changed.

### **Pathology**

The characteristic retinal changes are: frequent occurrence of papilledema, absence of exudates, lack of arteriovenous compression, normal arterioles, flame-shaped hemorrhages on, or adjacent to, the optic disc, and loss of vision out of proportion to the fundal changes. Ballantyne in his report cites four cases, in addition to his own, in support of his thesis that the initial disturbance is a central scotoma and papilledema followed by acute bulbar neuritis with blindness and retinal hemorrhage as the final stage. Whatever these changes, they are

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most certainly reversible, since in all the reported recovered cases, the blindness and retinal changes disappeared completely. We were most interested in the sharp retinal reversals which occurred in the case to be reported and which incidentally paralleled marked general physical changes.

### Treatment

It is generally recognized that the only hope these patients have for survival is prompt termination of the pregnancy as soon as retinal hemorrhage is recognized. Ballantyne has emphasized that the varying impairment of the visual fields which precedes gross hemorrhage may aid in determining an earlier and more opportune time for interruption before the patient is in extremis. Heroic supportive measures to establish a more normal blood chemistry are necessary before operative interference is attempted.

### Case Report

Mrs E. M., a 34-year-old, white, gravida ii, para i, was first seen by us in consultation, June 20, 1946. Family history was negative. Past history was not unusual except for an episode of vomiting of three weeks' duration following a normal pregnancy and delivery eleven years previously. This attack of vomiting ceased spontaneously and undiagnosed. History of present illness indicated an amenorrhea since April 19, 1946. Present pregnancy was uneventful until May 28, 1946, when she began to vomit daily. Vomiting followed no particular pattern, had no relation to eating, was accompanied by nausea, and occurred as often as every half-hour. She had received classical but inadequate treatment for approximately two weeks without improvement. Physical examination revealed an adult female in advanced state of dehydration, partially comatose, with temperature of 98.6 F., pulse of 90 per minute, respiratory rate of 20 per minute, and blood pressure 130/70. Salient physical findings were those of an intrauterine pregnancy of 10 to 12 weeks' duration with moderate myofibrosis uteri, and advanced diffuse hemorrhagic retinitis obscuring the disc and vessels. The blood count revealed 9.1 Gm. of hemoglobin and 4,000,000 red blood cells. The patient's blood was type A, Rh positive. A Friedman test had been reported positive. A diagnosis was made of hyperemesis gravidarum, severe, with retinal hemorrhage complicating intrauterine pregnancy. Interruption of the pregnancy was advised as soon as the severe malnutrition and dehydration could be combatted.

A vein was cannulized and, in the next twenty-four hours, the patient received 6,500 c.c. of fluids intravenously, consisting of 1,000 c.c. of sixth molar sodium lactate, 5,000 c.c. of 10 per cent glucose in normal saline solution, and 500 c.c. of whole blood. Sodium Luminal, Gm. 0.3, was administered parenterally in divided doses. On the following day the patient was somewhat improved clinically. Ophthalmoscopic examination revealed that, except for slight peripheral congestion, the diffuse hemorrhagic retinitis of the previous day had cleared. The optic discs were visualized and appeared normal. Normal arteriovenous ratio existed. No pinch crossings and no tortuosity of the vessels were noted. In view of the clinical improvement and with the establishment of relatively normal blood and urine chemistry, it was decided to postpone surgery for another twenty four hours in an effort to improve further the operative risk. By the next morning, June 22, 1946, it became clear that the optimal time for surgery had passed. The patient was again comatose, retinal hemorrhage reappeared as before, the pulse rate rose to 96, and the blood pressure reached 140/80. Under sodium Pentothal and oxygen, with concurrent infusion of whole blood and plasma, the uterus was emptied of a grossly normal ten-week fetus and secundines by dilatation and evacuation. The patient was so comatose that only 0.15 Gm. of sodium Pentothal were required. Intravenous therapy was continued for the next forty-eight hours. The most noteworthy fact in this regard was the administration, over a twenty-four hour period, of 34 Gm. of sodium chloride. Even this amount failed to increase the blood chloride level. Nothing by mouth was permitted during this period. Then followed a gradual transition to full diet. One other transfusion of 500 c.c. of whole blood



was given on June 28, 1946. Normal vision returned slowly over a period of days. The patient was discharged July 5, 1946. At this time and on subsequent follow-up visits, she exhibited no residual ocular or cardio-vascular-renal pathologic findings.

### Summary

This case presents the characteristic findings of severe hyperemesis with retinal hemorrhage except that, due to the comatose condition of the patient, visual disturbances could not be evaluated. It also illustrates the common pitfall of allowing temporary improvement to give one a false sense of security. We feel that, had she died, we might have been severely criticized for not interrupting the pregnancy twenty-four hours earlier. We cannot comment on the retrobulbar neuritis and other changes which Ballantyne indicates precede gross hemorrhage, inasmuch as we did not see the patient until retinal hemorrhage had developed. We concur with Stander that the hemorrhage is due to increased capillary permeability, associated with profound physical and chemical changes secondary to dehydration and inanition. These changes are reversible and not associated with permanent ocular or cardio-vascular-renal damage. The etiology remains obscure. Prompt termination of the pregnancy resulted in complete recovery.

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250 SOUTH EIGHTEENTH STREET

## HEMANGIOENDOTHELIOMA OF THE UTERUS\*

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**TUMORS** of blood vessel origin are believed to arise from previously formed capillaries, somewhat in the same manner as those produced in granulation tissue. The endothelial cells of these capillaries sprout to form solid cords which then become canalized.

Tumors of blood vessel type can be benign or malignant. Benign tumors are called angiomas and may be of capillary, cavernous, or venous type. They are very common, widely distributed throughout the body, occur in all ages, and are histologically characteristic of their type. Malignant tumors are called hemangioendotheliomas. They are quite rare—in occurrence and difficult of diagnosis. As far as we know, only one other case of this type has been reported as having occurred in the uterus.

Mrs. F. G., a 47-year-old white woman, complained that her menstrual periods, which ordinarily occurred regularly every twenty-eight days, were now, during the past two years, occurring every twenty-one to twenty-two days. The periods lasted five days, were of moderate amount and painless. She was gravida iii and para iii (children fourteen to twenty-six).

The past history revealed the occurrence of pneumonia in 1920. In 1932, the appendix was removed and a cystic left ovary was resected.

The vulva and vagina were normal. The cervix was cystic. The uterus was small, anteverted, and mobile. The left tube and ovary were normal. Right adnexa were firm and fibrotic (scarring). Rectal examination negative.

Urine: pH 6.5, albumin 0, sugar 0, specific gravity 1.020. Microscopically, 0 to 1 white blood cell, 1 to 2 epithelial cells. Pregnancy test: negative. Complete blood count: hemoglobin 14.6 Gm., red blood cells 4,960,000, white blood cells 10,100; neutrophils 71, leucocytes 25, monocytes 3, eosinophiles 1 (filamented 67, nonfilamented 4). Blood sugar: 80 mg. per cent. Blood urea nitrogen: 9 mg. per cent. Blood type: 0.

Sept. 14, 1945, a diagnostic curettage was done and demonstrated the presence of the tumor below described.

Sept. 16, 1945, a total hysterectomy and bilateral salpingo-oophorectomy were done under fractional spinal anesthesia. The organs were small, free in the pelvis, and not bound down by adhesions. The removal was uncomplicated, and the postoperative course uneventful.

*Pathologic Report.*—The first specimen consisting of endometrial scrapings was unlike anything we had previously encountered. The fragments were large, hard, and pale and where the endometrial surface was visible it was finely nodular. The second specimen, two days later, consisted of uterus, cervix, tubes and ovaries. The uterus measured 9 by 5 cm., the wall 2.5 cm. At the right cornua was a hemorrhagic mass 2.5 by 1.5 cm., a blood cyst within the tumor extended to within 2 mm. of the peritoneum at the fundus. A myoma, the size of a pea, was found in the anterior wall. The lining had been thoroughly curetted.

The tubes and ovaries showed nothing remarkable either grossly or microscopically.

*Microscopic examination, uterus:* In all, eight pieces were taken for paraffin embedding, four from scrapings, three from the tumor and adjacent muscle, and one from the uterine wall above the internal os. They were stained with hematoxylin and eosin and with

\*Presented at a meeting of the Philadelphia Obstetrical Society, Oct. 2, 1947.

Foot's reticulin stain. Seven of the sections included what would normally have been endometrium. In only one, that from above the internal os, were occasional endometrial glands found. Everywhere else, the endometrium was completely replaced by tumor. The tumor consisted of small irregular cells. Many were somewhat elongated, and here and there they could be seen to resemble the endothelial cells of blood vessels. The tumor was traversed by enormous numbers of capillaries lined by endothelial cells which in most places were obviously tumor cells. The cells tended to lie very close together; often the nuclei overlapped toward the lumen, sometimes they were heaped up so as partially or completely to occlude the vessel. Here and there they had a whorled arrangement. Many giant cells consisting of clusters of nuclei were seen. Hemorrhages were numerous.

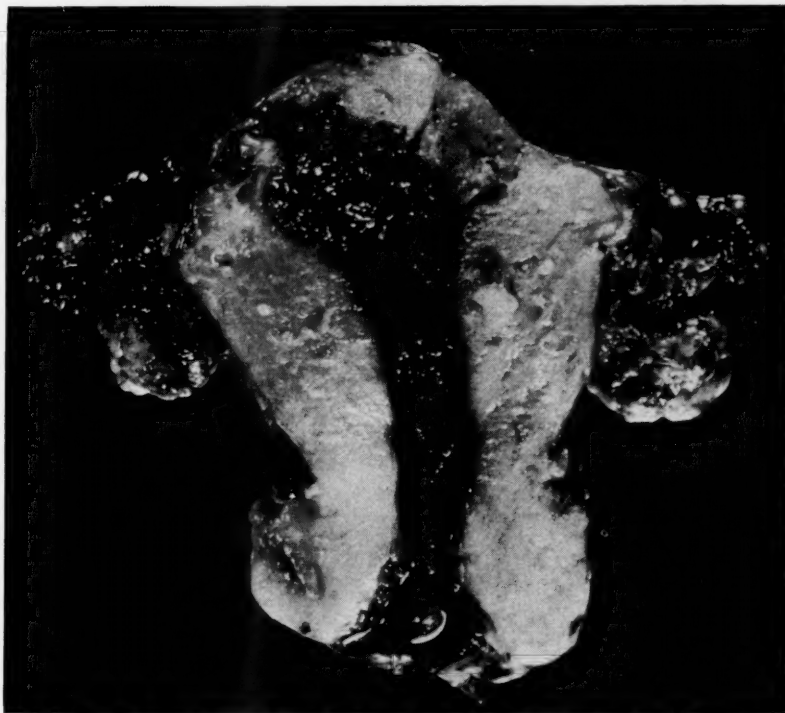


Fig. 1.—Hemangioendothelioma of uterus showing tumor invading the cornua of the uterus.

The reticulin stain showed characteristic capillary anastomoses which in the hematoxylin and eosin sections were obscured by the tumor cells. The tumor presented a well-marked reticulin framework in all the sections stained.

*Diagnosis.*—Hemangioendothelioma malignum.

### Discussion

The gross and microscopic pictures leave little doubt that we are dealing with a malignant tumor. Stout gives as criteria for malignant hemangioendothelioma: first, the formation of atypical endothelial cells in greater numbers than are required to line the vessels with a simple endothelial membrane; and, second, the formation of vascular tubes with a delicate framework of reticulin fibers and a marked tendency for their lumina to anastomose. Both these criteria are fulfilled in our tumor. Grossly, infiltration of the endometrium was widespread and obvious. Infiltration of muscle was certainly present. We attribute the lack of metastases to the fact that malignant tumors of the uterus, especially of the fundus, tend to metastasize relatively late; and, second, that in this case the uterus was removed before

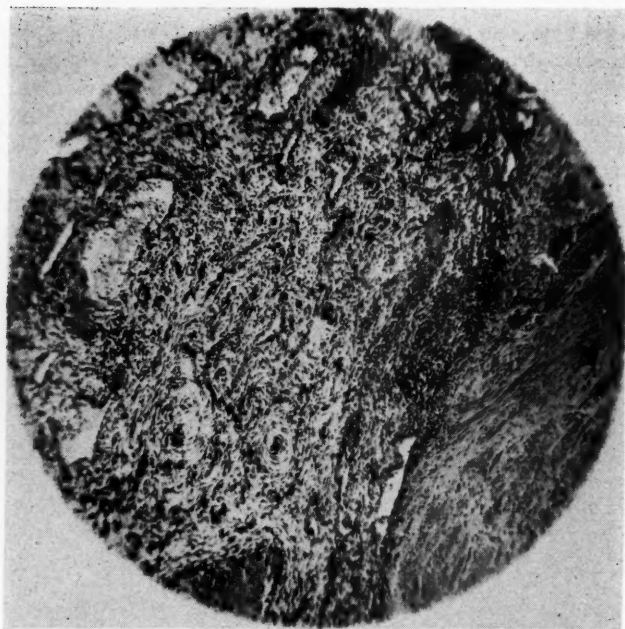


Fig. 2.—Hemangioendothelioma of the uterus showing endometrium replaced by tumor.  $\times 100$ .

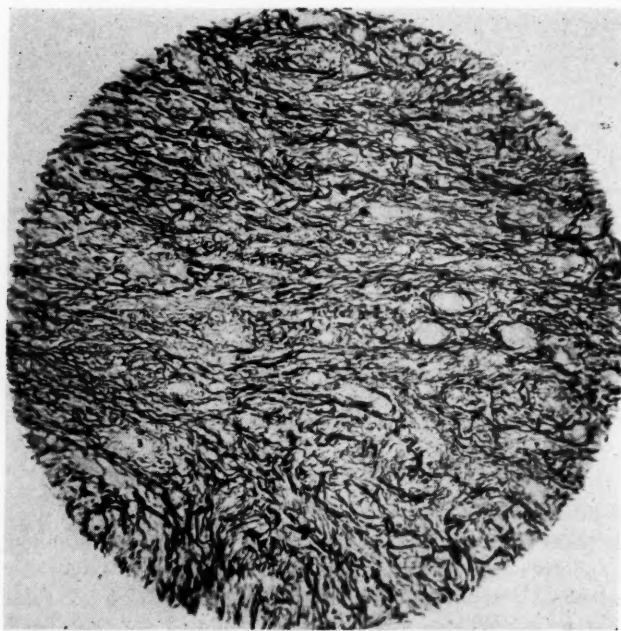


Fig. 3.—Hemangioendothelioma of the uterus showing capillary formation  $\times 200$ . Foote's reticulum stain.



there had been symptoms attributable to the tumor. The diminished intermenstrual time or shortened cycle cannot be attributed to the presence of a tumor, but rather to a beginning of menopause.

The patient has been examined repeatedly since the operation, and so far, has been found to be in excellent condition. She is active and working regularly without any complaints. The last pelvic examination, done July 25, 1948, showed a normal vulva and vagina. The vault of the vagina was held high; there was no evidence of a prolapse. The uterus, both tubes, and ovaries were absent. No pelvic or rectal pathology was felt.

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## ABSENCE OF TUBE AND OVARY, CONGENITAL OR ACQUIRED

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**T**HIS patient was operated upon by the writer when in charge of the Gynecological service at a Veterans Administration Hospital, and is reported because it presents an etiological problem not conclusively solved and an unusual operative finding which has not been given much attention in textbooks or the literature.

Congenital abnormalities of the vagina and uterus are not uncommon by contrast with abnormalities of development of the urogenital system and the development of the Müllerian ducts and their subsequent fusion from the caudal portion cephalad, starting at the Müllerian tubercle, will account for the more frequent development of abnormalities in the vagina and uterus. Congenital absence of an ovary is not common,<sup>1</sup> but does occur, as may also accessory ovaries. Embryologically there is little or no reason for absence of a tube to be accompanied by absence of the corresponding ovary, since the ovary develops from the celomic mesothelium and underlying mesoblastic stroma quite apart from the Müllerian duct which arises as a tubular invagination of the cells lining the celom, the orifice of the invagination remaining patent to form the abdominal ostium of the uterine tube.<sup>2</sup>

Whether the case to be presented is one of congenital absence of the tube and ovary or of later acquired absence due to an inflammatory process is not determined.

**History.**—The patient, A. P., white, aged 22 years, single, was admitted with a complaint of irregular bleeding and pain in the right lower quadrant for the past one and one-half years. Menarche at 15 years, regular in character, every twenty-eight days, but with a moderate flow for only one day. Metrorrhagia in March and April, 1947.

One and one-half years ago, while on duty in the Womens Army Corps, the patient noticed pain when walking or on exertion. A tentative diagnosis of a cyst of the right ovary was made at an Army Hospital, though opinions differed. She was discharged, unoperated upon, but experienced intermittent pain. Although periods had always been regular but of only one day's duration, she flowed from March 22 for eight days and then irregularly until April 22. While flowing excessively in March and April, 1947, the patient states that she had fever. She has had a white vaginal discharge, nonitching, for the past year.

This patient had an abortion in October, 1946, at the fourth month of gestation. This was followed by peritonitis for which she was treated at home with penicillin and medicines. She was in bed for one month.

**Physical Examination.**—Vulva negative. Vagina: frothy, yellowish white discharge. Cervix in axis of vagina, erosion of posterior lip, os small. Corpus: 4 cm. in size, dextro-rotated and anterior, normal consistency, regular outline, limited motion. Adnexa: on the right side there is a diffuse, tender mass, circa 4 to 6 cm., narrower at the cornual end, the ovary cannot be differentiated. Left adnexa: no tubal thickening, ovary small.

**Laboratory.**—Urinalysis, blood count, bleeding time, coagulation time normal. Sedimentation rate 9 mm. per hour. Blood chemistry normal. Serology negative. Cervical culture and smear showed Döderlein's organism predominating. Urethral culture showed diphtheroids, nonhemolytic *Staphylococcus aureus* and *Coliform bacillus*. *Trichomonas vaginalis* present.

**Impression.**—(1) Chronic salpingitis or (2) possible ovarian cyst, right.

**Operation and Findings.**—Under general anesthesia, through a midline incision, the abdomen was opened. The right tube was the site of a chronic salpingitis, manifested chiefly by an enlargement of the ampulla and fimbriated end. The fimbria were closed, and the outer

half of the tube was enlarged and nodular, with some fine adhesions to the right ovary, which, however, appeared free of infection and normal. On the left side there was no evidence of ovarian tissue. A small thickening about 1 cm. in length, with a closed blunt end extended from the left cornua and was the only evidence of a left tubal structure. On the floor of the pelvis, anterior to the anterior leaf of the right broad ligament, a hard somewhat yellowish plaque was seen. This measured about 16 mm. by 12 mm. by 3 mm. This was attached to the pelvic peritoneum by a few fine adhesions, and was readily lifted off the peritoneum. The corpus uteri was small, firm in consistency, and regular in outline, infantile in type, 3 to 3½ cm. in length, and the cervix about 4 cm. in length.

A right salpingectomy, panhysterectomy, and appendectomy were performed.

*Pathologic Report.*—Gross: The specimen consisted of uterus and cervix with the right tube attached. The uterus was small, measuring 7 cm. in length and 4 cm. in maximum diameter. The wall measured 10 mm. in maximum thickness and was lined by a thin layer of pale translucent endometrium. The cervix was not remarkable. The right tube measured 9 cm. in length. The lateral extremity was reflected back and adherent to the ampulla, the tube in this region measuring up to 1 cm. in diameter. The fimbriated end appeared closed, and was covered over by adhesions. In the left cornual region appeared a slight projection of nondescript tissue which had been previously cut through. Also submitted was a flat discoid calcified structure, 20 by 13 by 3 mm. An appendix 7 cm. in length was also submitted and was not remarkable.

*Microscopic.*—Sections of the uterus disclosed a nonsecretory type of endometrium with regular glandular pattern. The myometrium was of less than normal thickness, but not otherwise remarkable. The endocervix showed a mild chronic inflammatory infiltration. Sections of the right tube displayed thickened, adherent plicae with a diffuse infiltration of lymphocytes, plasma cells, and eosinophiles, involving all the coats of the wall. A similar infiltration was noted in the left cornual region in the stump of tissue seen here grossly. The appendix was patent, and its wall showed mild lymphoid hyperplasia. Sections of the decalcified loose body from the pelvis disclosed a thick hyalin capsule suggesting that the structure represented a lymph node. The enclosed material was granular or amorphous with numerous acicular clefts, indicating the presence of lipids. No other tissues or structures were identifiable. Studies of this material failed to offer a reasonable explanation for absence of the left tube and ovary. The loose body appeared to be a calcified lymph node rather than an ovary or a lithopedion which had been considered.

*Diagnosis.*—Chronic salpingitis, hypoplasia of the uterus, follicular type endometrium, chronic endocervicitis, chronic lymphoid appendicitis, calcified lymph node (tuberculous?).

*Comment.*—The previous surgical removal of the left ovary and outer portions of the left tube is ruled out by the fact that this patient had not been operated upon either per abdomen or per vaginum if one can exclude the previous abortion which was performed by either a nurse or midwife, was of only a few minutes' duration and performed at home.

The possibility of the absence being accounted for by sloughing of the ovary and most of the tube, as a result of an inflammatory process, cannot at present be denied and seems not too unlikely, though the history gives no indication of a previous severe salpingoophoritis. That this patient had a salpingitis prior to her abortion is obvious, but close questioning gave the impression that it was not of great severity and was misdiagnosed while in the Army as a small ovarian cyst—scarcely a likely mistake if the infection were severe enough to cause sloughing—furthermore the symptoms and findings at all times were purely right-sided. Now considering the possibility that the sloughing occurred post abortal, we must note that the "peritonitis" was not severe enough to require hospitalization, and the patient insisted that during this illness her pain was entirely right-sided.

The hypoplasia of the uterus which was definitely infantile in type, the cervical portion being longer than the corpus, casts a shadow on the diagnosis of a previous pregnancy.

At the time of operation and when examined grossly by the pathologist, it was thought that the calcified plaque was a calcified ovary, but tissue examination did not bear this out.

Accordingly, we must assume that both tube and ovary sloughed and were absorbed or that both were congenitally absent, and the writer believes sloughing the most likely cause, but the history denies the expected previous severe illness.

The author regrets that a complete urological study was not made to rule out possible congenital urinary anomalies which might have been found if the absence of the tube and ovary were congenital in origin.

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## UNIUMBILICAL-DIBRACHI-DICEPHALIC MONSTER; ROENTGENOGRAPHIC DIAGNOSIS IN UTERO, DELIVERY BY LOW CLASSICAL CESAREAN SECTION\*

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ORDINARILY the delivery of a monster is not of sufficient interest to warrant report. However, we have not been able to locate any other instance of the diagnosis of a monster of this type in utero and of its subsequent delivery by section under circumstances so favorable for the mother. Indeed certain authorities, notably DeLee, say that this has never taken place.

The usual sequence of events in this obstetric dilemma is for the diagnosis to be entertained only when labor has been long in progress, and the second stage does not develop as expected. After such exposure to exhaustion and to manipulation, it is not surprising that operative procedures, whether destruction or cesarean, are attended with high maternal mortality.

We feel that the sensational aspects of this problem are less important than the practical problem of diagnosis of monsters, the delivery of which by the vaginal route is obviously fraught with the gravest maternal consequences. A careful search of the usual sources has revealed no other instance in which a full-term monster of the uniumbilical-dibrachi-dicephalic type has been diagnosed by prophylactic roentgenography while yet in utero so that cesarean section might be truly elective in every sense of the word.

We wish also to emphasize the relatively atraumatic experience this patient has had, as compared with other cases reported in the literature. Her surgical risk was minimal and her psychic trauma does not seem to have been great enough to discourage her from trying to become pregnant again.

*History.*—Mrs. J. O., a white married primiparous female, was first seen (J. D'A.) on March 1, 1947. Her history and her physical findings were consistent with those of a two months' pregnancy.

Prenatal findings continued to be entirely normal until about three weeks before the expected date of confinement. At that time abdominal palpation suggested the diagnosis of a twin pregnancy. Two masses, the size and consistency of which suggested (in a parous woman near term) that they were heads, were clearly made out. One was at the pelvic inlet in a position consistent with the last month of pregnancy, the other, apparently of equal size, was in the lower left quadrant, somewhat out towards the flank.

The patient was then referred for roentgen studies. The radiologist (C. M. L.) made the startling diagnosis of a dicephalic monster on the basis of extensive studies. At the time (Sept. 8, 1947) he commented: "Examination of the abdomen in the anteroposterior and lateral projections reveals a twin pregnancy, in the third trimester, one fetal head overlying the pelvic fossa and the other close by in the midabdomen. Because of the unusually close approximation of the fetal vertebral columns, particularly in the lower dorsal, lumbar and sacral areas, right and left posterior oblique exposures were then made. These bear out the constant close approximation of the vertebral columns, revealing only one fetal pelvis, one pair of lower extremities and one pair of upper extremities.

"The maternal pelvis of the gynecoid type and normal in appearance.

"*Conclusion:* Radiologically viable twin pregnancy conjoined from thoracolumbar region distally to a single pelvis."

It was decided to deliver the patient at once by section through a low classical incision. It was thought that this would be the best approach from which to enlarge a uterine incision should the unusual size, shape, or position of the fetus so require. Fortunately this was not the case. The abdominal head was delivered with ease, the pelvic head followed readily, as did the rather broad torso, all with a minimal amount of manipulation. The placenta detached spontaneously and the patient's convalescence was optimal.



Fig. 1.—Uniumbilical-dibrachi-dicephalic monster immediately post partum. Death ensued within the hour.

The monster lived for about an hour, dying just as an electrocardiogram was being attempted. Autopsy was allowed.

*Autopsy Findings.*—The body was that of a robust male infant with two well-shaped heads and necks set on a single pair of somewhat broad shoulders. The duplication began pectorally, the superior skeletal abnormality being a V-shaped bone which seemed to be fused from scapular anlage. Clavicals were not found.

Two well differentiated vertebral columns continued down to the sacra and were held together, at each rib-level, by a small mutual rib joining the two vertebra so that a large thoracic cage was formed by the lateral ribs of each side and the bridging element.

The duplication was even more remarkable internally. The anatomic structures normally found in the throat and the superior mediastina were present and duplicated. The thymus in

each neck was normal, but displaced laterally somewhat. Equal duplication ceased at the level of the stomachs. The right esophagus emptied into a small stomach situated below and behind the large single liver. The left esophagus and a left stomach were of the type usually seen. The pylora of the stomachs gave onto a double-barrelled duodenum and jejunum, the right element being somewhat smaller and less well defined. The duplication of the ileum was more distinct, each having a small mesentery split off the attachment to the posterior abdominal wall. The cecal-anal bowel was single and not remarkable.

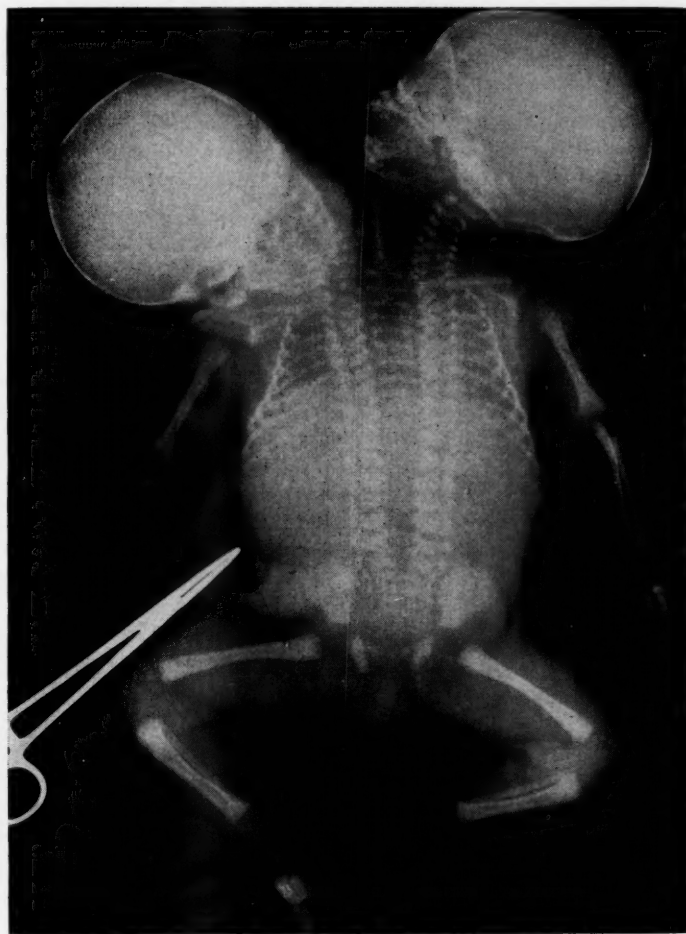


Fig. 2.—Postmortem roentgenogram.

In the thorax each trachea connected with a complete set of lungs crowded into its respective side of the cage. There were two hearts. One, sinistrad, was not remarkable except perhaps that the aortic arch arising from it was somewhat thinner than usual. The pulmonic artery went to the left set of lungs. The second "heart" was dextrad, bilocular, about the size and shape of that of a domestic fowl. From its apex it was attached by a nonpatent fibrous cord to the right auricle of the left heart. From its auricular aspect arose a delicate aorta, the arch of which was poorly defined and the pulmonary artery of which was directed towards the right set of lungs.

The liver was single, perhaps somewhat large, but remarkable only for the presence of two gall bladders and two biliary duct systems, each of which led to its respective duodenum. The pancreas was duplicated, that associated anatomically with the right stomach was somewhat smaller.

(The other organ systems were investigated but were in no way remarkable.)

Extreme care was taken to spare the mother reference to a "two-headed monster" and to keep the whole episode as emotionally flat for her as was possible. She has later been able to accept a frank statement about the nature of the infant born to her; that she had "twins which were joined at the trunk" and which had not survived.

### Summary

A primiparous white female was thought to have a twin pregnancy. Roentgenographic studies revealed the presence of conjoined twins which were delivered by elective low-classical cesarean section. The monster lived but an hour. The mother's convalescence was not remarkable.

While only of remote value in obstetric diagnosis, this case report illustrates the value of roentgen studies in all cases in which any deviation from the usual is suspected. We consider these studies to be particularly indicated before decision for elective cesarean section is definitely made.

We are indebted to Dr. Charles R. Kingsley, Jr., for advice and suggestions and to Dr. Madeline Penke, Pathologist, who performed the necropsy.



## POSTMORTEM CESAREAN SECTION AFTER DEATH FROM BULBAR POLIOMYELITIS

### Report of Two Cases With Living Infants

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A STUDY of the literature fails to reveal any report of postmortem cesarean section on pregnant women dying of poliomyelitis. It is the purpose of this paper to present two such cases, both of which produced living children.

### Case Reports

CASE 1.—(C. G. H. No. 74385), Mrs. F. C., a 31-year-old, white, gravida viii, para vii, was admitted to Colorado General Hospital on Aug. 8, 1946. Her last menstrual period had occurred in January, 1946. Her admission complaints were of neck pain of two days' duration, and of dull precordial pain for about the same length of time. She had vomited once. There had been numbness and tingling of the left hand for several hours. Seven previous pregnancies and deliveries had all been uneventful. Additional relevant history was that one of her six living children had died of acute anterior poliomyelitis in this hospital nine days before her admission.

On examination she was acutely ill, manifesting extreme dyspnea and marked orthopnea. Her extremities were cold and cyanotic. There was mild nuchal rigidity. There was weakness of the left arm. Respiratory efforts necessitated use of the accessory muscles of respiration. Intrinsic chest musculature moved but slightly. She was unable to swallow, and could not cough. The uterus was gravid, the fetus estimated at thirty-six weeks' gestation in vertex presentation, unengaged. Fetal heart tones were faint and irregular in the right lower quadrant. There seemed to be polyhydramnios.

Admission laboratory studies of significance were confined to the spinal fluid which contained 1,700 cells per cubic millimeter, with a differential count of 75 per cent polymorphonuclears and 25 per cent lymphocytes. There were 75 milligrams per cent sugar and 75 milligrams per cent protein. Admission diagnoses were: acute poliomyelitis with bulbar involvement, and uterine pregnancy, undelivered, near term.

The patient's course was steadily downhill after admission, with increasing cyanosis and more labored respirations despite supportive therapy. Within six and one-half hours after admission she was moribund, and preparations were made for postmortem cesarean section. Without delay after her death a classical section was performed, revealing a twin pregnancy. The first infant was delivered forty-five seconds after death of the mother, and his twin about two seconds later.

Twin boy No. 1, C. G. H. No. 74397, weighed approximately 1,800 Gm., voided immediately after delivery, but did not make any respiratory effort for twenty minutes. During this period postural drainage, mouth to mouth breathing, and suction, were employed. With the continued efforts the infant finally began to breathe by himself. He did very well until the twelfth day of life when he regurgitated a small amount of feeding and became cyanotic. Despite therapy he grew progressively worse and died on his thirteenth day of life.

Twin boy No. 2, C. G. H. No. 74398, weighed approximately 1,500 grams. After delivery he made no respiratory effort despite prolonged resuscitatory attempts, and no heartbeat could ever be heard. During resuscitation excessive amounts of amniotic fluid were drained from his nose and mouth.

Significant pathologic findings in the postmortem examination of the mother (C. G. H. Path. No. 46-189) were in the central nervous system, which showed the typical findings and pathologic changes of acute bulbospinal poliomyelitis. The pathologic diagnoses were poliomyelitis, acute bulbospinal type, myocardial hemorrhages, and edema of the lungs.

At autopsy twin boy No. 1 (C. G. H. Path. No. 46-198) weighed 1,680 grams. There was complete atelectasis of the posterior and basal portions of both lungs, with scattered atelectatic areas throughout the remainder. The brain weighed 210 Gm., and showed vascular congestion of the white matter mainly in the parietal lobes, and hemorrhagic infiltration of the choroid plexus. Microscopically there were large atelectatic areas, and areas of emphysema, in the lungs. The brain and spinal cord revealed no evidence of poliomyelitis, but did show degenerative anoxic changes of the nerve cells of the cerebral gray matter, particularly in the thalamus, with multiple petechial hemorrhages in the cerebral white matter. The pathologic causes of death were prematurity and atelectasis.

Twin boy No. 2 (C. G. H. Path. No. 46-188) weighed 1,660 grams. Cyanosis of the body surfaces was pronounced. There were subepicardial hemorrhages around the great vessels at the base of the heart. The brain showed meningeal hyperemia. Microscopically there were small epicardial hemorrhages which reached into the myocardium. Most of the lung alveoli were unexpanded, although some were partially dilated with fluid, blood, and numerous epithelial cells. Bronchioles contained similar material. There was no microscopic evidence of inflammatory alteration of the brain or spinal cord due to poliomyelitis. Pathologic causes of death were given as prematurity, bilateral atelectasis, and focal hemorrhages into the heart, lungs, kidneys, and thymus.

CASE 2.—(C. G. H. No. 74580) Mrs. L. S., a 23-year-old white gravida iii, para ii, was admitted to Colorado General Hospital on Aug. 21, 1946. Her last menstrual period had occurred in December, 1945. Her admission complaints were of aching in the neck and shoulders of thirty-six hours' duration, and a throbbing headache for twelve hours. There had been some diarrhea for two days, and the patient complained mildly of generalized weakness. She had had two previous term pregnancies with normal deliveries and uneventful puerperia.

Physical examination revealed a well-developed young woman who did not appear to be acutely ill. There was some flatter of the spinal muscle mass in the thoracic region. Nuchal rigidity was moderate. Deep tendon reflexes were normal. The abdomen was distended by a gravid uterus estimated to contain a fetus of about thirty-four weeks' gestation, in left sacroposterior position, unengaged. The fetal heart tones were loud and regular at 140 per minute in the left lower quadrant.

Pertinent laboratory findings were confined to the spinal fluid which contained 420 cells per cubic millimeter with a differential count of 50 per cent polymorphonuclears and 50 per cent lymphocytes. Spinal fluid chemistry showed 64 milligrams per cent sugar and 55 milligrams per cent protein. Admission diagnoses were: acute anterior poliomyelitis and uterine pregnancy, undelivered.

The patient's hospital course was good for the first forty-eight hours. After this interval she began to show respiratory distress with increased voluntary effort, and beginning cyanosis of the extremities. Respiratory distress increased, and fifty-six hours after admission she was placed in a respirator and given endotracheal oxygen. During the following five days there were no changes in her condition. There was never any evidence of fetal distress on repeated examination. On her seventh hospital day she became critically ill, with fever of 104° F., and periods of coma. She manifested involuntary coarse twitchings of the facial muscles. Pulmonary congestion with basal râles and tracheal rattling developed, and shortly after this, she expired without ever having been removed from the respirator.

Postmortem cesarean section was immediately done using the classical technique. A viable female infant weighing approximately 2,800 Gm. was delivered within thirty seconds after the maternal death. The infant was limp and cyanotic but, with mild stimulation and suction, began to cry lustily. Her condition was quite good, despite occasional spasmodic twitchings of the extremities which appeared eight hours after birth and persisted for the next three days. There was never any evidence of central nervous system disease on repeated examinations. She was kept under observation in the hospital for twenty-five days. On discharge she had gained 1 pound, 2 ounces, and she was taking an evaporated milk formula well. Since then she has been followed in the outpatient clinic, and continues to do well.

Postmortem pathologic studies on the mother of this infant (C. G. H. Path No. 46-206) revealed no gross findings of note other than the operative incision. Microscopic examination showed edema of the trachea with infiltration of polymorphonuclear leucocytes and lymphocytes. The lungs contained much fluid, and foci of alveoli were filled with erythrocytes, neutrocytes, and monocytes. An incidental finding was slight edema of the appendix with polymorphonuclear and lymphocyte infiltration. The brain showed diffuse focal areas of infiltration, especially about the dentate nucleus, with perivascular infiltration and small hemorrhages. In the pons these same changes were noted and, in addition, glial proliferation, glitter cells, and early softening were seen. The nuclei of the vagus and hypoglossal nerves were involved, as were the basal ganglia. In the cerebellum perivascular infiltration and microglia were prominent. There was hyperemia of the cerebrum with infiltration of polymorphonuclears, lymphocytes, plasma cells, and considerable glial reaction. Pathologic diagnoses were: Acute anterior poliomyelitis, bulbospinal type, subacute tracheobronchitis, and subacute appendicitis. Sections of the lumbar and cervical cord from this patient were reported as positive for the presence of the poliomyelitis virus.

### Comment

Our experience confirms the findings of McGoogan<sup>3</sup> and Grelland,<sup>4</sup> since none of our three infants showed evidence of intrauterine transmission of poliomyelitis from mother to infant.

There is little doubt that the loss of the second twin in the first case in our series was due to intrauterine asphyxia with aspiration of amniotic fluid because of the prolonged period of respiratory embarrassment in the mother prior to her death. The successful result in the second case must have been due to adequate oxygenation of the mother up to the moment of her death. It is interesting to note in retrospect that the fetus in utero in no way interfered with the use of the respirator, nor did the respirator appear to have any untoward effect on the infant.

The poliomyelitis epidemic in Colorado in 1946 showed that pregnancy is no protection against poliomyelitis, and, in fact, it revealed that pregnant women were twice as susceptible to the disease as their nonpregnant sisters.<sup>5</sup> During the same epidemic the mortality rate in patients in the last trimester of pregnancy with acquired poliomyelitis was 50 per cent.<sup>5</sup> Should another epidemic of such proportion arise it will be valuable to know that it is possible to save some babies that would otherwise perish.

We wish to acknowledge our indebtedness to the various members of the Department of Pathology of the University of Colorado Medical Center for their assistance in the pathologic reports included in this paper.

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638 REPUBLIC BLDG., DENVER, COLO.  
131 NUSBAUM, SANTA FE, N. M.

## CARCINOMA OF BARTHOLIN GLAND DUCT\*

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CARCINOMA of Bartholin's gland is considered so rare that it is usually recognized too late to be successfully treated and the diagnosis is seldom suspected before surgical intervention. Simendinger collected only 38 cases of primary carcinoma of Bartholin's gland and, of these, 29 cases were adenocarcinoma and 9 were squamous-cell carcinoma. The latter presumably arose from the duct. Cosbie found one carcinoma of Bartholin's gland in 57 cases of carcinoma of the vulva and in Taussig's series of 155 vulvar carcinomas, 9 originated in Bartholin's gland.

Most authors agree that early metastases to inguinal lymph glands occur and recurrence is common, with poor prognosis in all carcinomas of Bartholin's gland.

The majority of cases occurred between the ages of 40 and 55. There is a divergence of opinion as to whether or not infection is a predisposing factor. Simendinger and Hoffman did not consider it to be a factor, while Taussig, in his later report, found that infection was definitely present in four of nine Bartholin gland carcinomas.

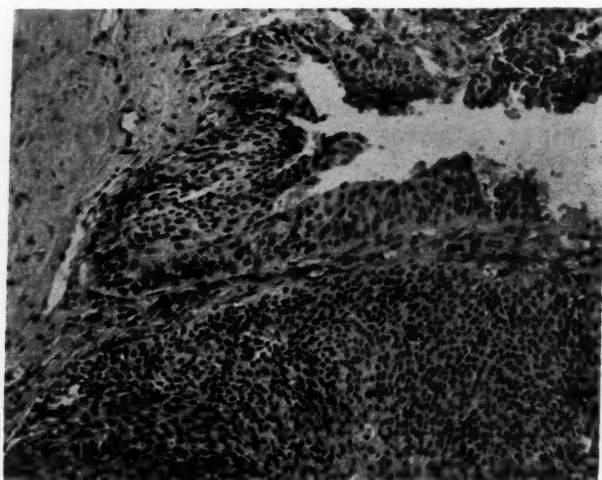


Fig. 1.—Carcinoma of Bartholin gland duct, showing area of multilayered transitional epithelium.

Patient, aged 57 years, noticed a swelling in the lower right side of the vagina for the past year. There was no open ulcer, no bleeding, and no discharge. Examination of the abdomen was negative except for vague tenderness in the right lower quadrant. One deep femoral gland could be palpated on the right side. No perirectal glands were palpable.

The tumor, which was the size of a walnut, was located in the right Bartholin gland and was markedly adherent to the surrounding tissues.

Local excision of the tumor was performed in February, 1945. On histologic examination, one finds striated muscle of the bulbos cavernosus in the surrounding tissue. Many irregular-shaped heaps of multilayered transitional epithelium are present in the tumor.

\*Presented at the meeting of the Minnesota Society of Obstetrics and Gynecology at Duluth, Minn., May, 1946.



The nuclei are irregular and, for the most part, are oblong in shape. There is no adenomatous pattern in any portion of the specimen. One does not see any normal structure of Bartholin's gland or its duct. (The late Dr. Robert Meyer who reviewed the slides felt that there was no question that the tumor was a carcinoma of the duct of Bartholin's gland.)

A few days after local excision, a radical vulvectomy with excision of the superficial and deep inguinal glands on both sides was done, with removal of a part of the vagina above the tumor. On examination, the glands showed inflammatory reaction.

In November, 1945, the patient returned with a local recurrence in the posterior fourchette on the right side, which was excised and showed carcinoma of the same type.

The patient was alive in April, 1948, with no local recurrence of the tumor.

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1111 NICOLLET AVENUE

## PROLONGED PREMATURE RUPTURE OF MEMBRANES

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PREMATURE rupture of the membranes occurring several weeks before the onset of labor is infrequent. Whenever it is suspected the observer must evaluate the probable site and completeness of the opening in the amniotic sac and the possible influence on continuation of the pregnancy. As a general rule the lower the site of rupture the more abrupt and copious is the fluid escape—in the higher ruptures there is usually a “dribbling” of fluid, containing small flakes of sebaceous material. It is in this latter type that both the diagnosis and prognosis are more difficult and uncertain. In a few such instances the opening in the amniotic sac will heal, and the duration of pregnancy will be unaffected. In most cases labor will ensue at varying periods. We present a case report of proved premature rupture of the membranes, thirteen weeks before labor and delivery.

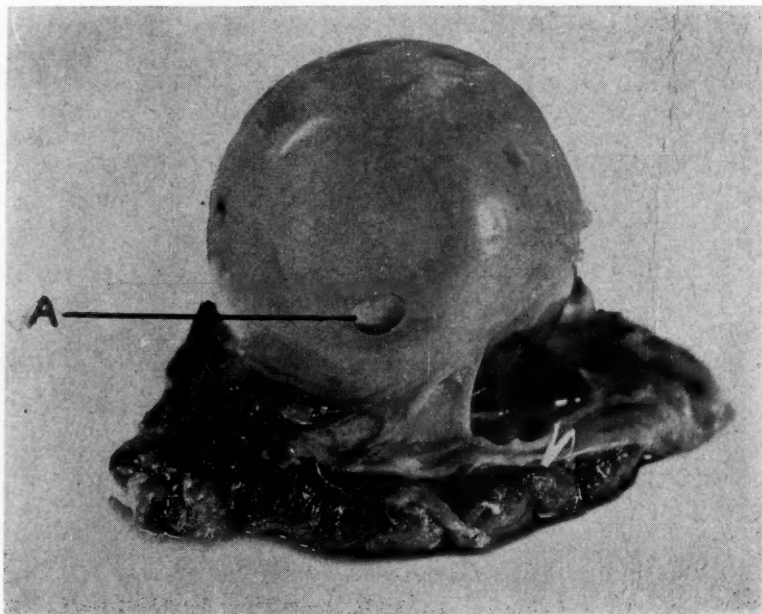


Fig. 1.—A. Site of rupture in the amniotic sac.

M. M., aged 28 years, white, gravida i. Her last menstrual period began Dec. 24, 1944; the estimated date of confinement was Oct. 1, 1945.

When first seen May 4, 1945, physical examination denoted a normal healthy woman with intrauterine gravidity of sixteen to seventeen weeks' duration. Fetal heart sounds were not audible.

On May 7 a sudden gush of clear fluid escaped from the vagina, followed by several similar emissions within the next twenty-four hours. There was no pain or bleeding. The patient was given 30 mg. of Pranone orally daily in an attempt to render the uterus less irritable. During the subsequent twenty-four hours of observation no further fluid was seen. The uterus was not irritable, and fetal heart sounds were distinctly audible. The cervix was uneffaced and undilated. Pranone therapy and bed rest, except for bathroom privileges, were advised. Tub baths, douches, and intercourse were forbidden.

On May 24 there was a similar sudden gush of fluid and fluid continued to escape in varying amounts, sometimes requiring the use of five pads daily. The fundus measured 19 cm., and the fetal heart sounds were still normal.

Labor began Aug. 15, 1945, and terminated with frank breech decomposition and extraction under pudendal block and nitrous oxide analgesia following left posterolateral episiotomy. The child cried vigorously and was apparently normal in development. It weighed 2,044 Gm.; the length was 38 cm., and the fetal course was uneventful following initial incubation and oxygen therapy. The child on discharge from the hospital was normal, weighing 6 pounds, 8 ounces. The maternal postpartum course was uncomplicated and afebrile.

The placenta measured 15 cm. in diameter. In the amniotic sac approximately 5 cm. from the periphery was a sharply delineated circular opening 1 cm. in diameter. The edges of the opening were smooth and round. Microscopic section of the amniotic sac across the opening showed "the edges to be covered with a membrane similar to the covering of the rest of the sac." (Fig. 1.)

## Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK, M.D., NEW YORK

### Review of New Books

#### Gynecology

It seems but a short time since I reviewed the fourth edition of Berkeley and Bonney's **A Textbook of Gynaecological Surgery** but upon investigation, I find that five years have elapsed. Now the fifth edition appears by Bonney<sup>1</sup> alone as Sir Comyns Berkeley has died. More than ever the book bears the personal imprint of Bonney, the versatile and distinctive surgeon who has illustrated the volume with his own simple and direct line drawings (590 illustrations). The book is meant for the surgeon who performs gynecological operations only now and then, but has an equal appeal for the gynecologist who wants to refresh his memory on some phase of an operation with which he is well acquainted. Anyone who has watched Bonney's uncanny skill at the operating table, his dexterity and speed, will find some of this individuality within the pages of his book. There may be no particular need for the special instruments and gadgets which the author has invented and uses, such as the vaginal clamp, dissecting forceps, wrist-reel, etc.

Bonney uses Indoe's technique in the inlay grafting operation for absence of the vagina. I agree with Bonney that the Baldwin operation for absent vagina might well be omitted from the next edition. The author advocates an orificial plastic operation for vaginismus (Fenton's). He might have devoted a few words to the selection of cases and the nonoperative treatment which is far more frequently applicable. Various techniques for vesicovaginal fistula operations are described, including transplantation of the ureters into the colon as a last resort. Cervical and intrauterine operations are detailed. I am pleased to note that Bonney favors supravaginal hysterectomy unless there are cogent reasons for removing the cervix, and also abdominal over vaginal hysterectomy. However, both vaginal and abdominal hysterectomy are depicted minutely.

The author's unique experience with the Wertheim operation and his description of this alone would make this book worth while. Another field, in which he has been a pioneer, is that of myomectomy. The chapter on cesarean section is complete.

In anterior colporrhaphy, neither the dissection nor the method of suture takes full cognizance of the anatomical structures; this applies as well to the depiction of the Manchester operation for prolapse. I note with surprise that a patient after a Le Fort operation is kept in bed twenty-one days. As I reserve this operation for the debilitated and aged, my practice is to get them up by the third day! For recurrent cases of stress incontinence of urine, he uses Terence Millin's modification of the Stoeckel-Goebell pro-

<sup>1</sup>**A Textbook of Gynaecological Surgery.** By Victor Bonney, M.S., M.D., B.Sc. (Lond.), F.R.C.S. (Eng.), Hon. F.R.A.C.S., Hon. F.R.C.O.G., M.R.C.P. (Lond.). Consulting Gynaecological and Obstetric Surgeon to the Middlesex Hospital; Consulting Surgeon to the Chelsea Hospital for Women; Honorary Consultant on Gynaecology and Obstetrics to the Army; late Visiting Gynaecologist to the British Postgraduate Medical School; late Gynaecological Surgeon to the Royal Masonic Hospital and Queen Alexandra's Hospital, Millbank. Late Member of Council and Vice-President of the Royal College of Surgeons of England. Sometime Member of the Central Midwives Board and Examiner in Diseases of Women and Midwifery to the Conjoint Board of England; Hon. Fellow of the American Gynaecological Society; Hunterian Professor, 1978-38-31, Bradshaw Lecturer, 1934, and Hunterian Orator, 1943, Royal College of Surgeons of England. Formerly Emden Research Scholar Cancer investigation Laboratories, Middlesex Hospital. Fifth Edition. With 590 original drawings by Victor Bonney and 17 colour plates. 928 pages. Paul B. Hoeber, Inc., New York, 1948.



cedure, the entire operation being performed from above. To my surprise, he still uses ventrofixation in some cases of prolapse, and describes two round ligament shortening operations and one of his own.

Space prevents me from giving details on his operations for ovarian cysts, for relief of tubal closure by implantation, and for myoma and pregnancy. There are chapters on intestinal surgery, including on abdomino-vaginal excision of the rectum, drawing the bowel through the split posterior vaginal wall. The concluding chapters deal with post-operative treatment, transfusion, postoperative complications of every variety, the repair of ventral hernia, etc. Little more than mere mention of penicillin is made. Mortality statistics as well as remote sequelae conclude this volume, which is of unusual interest and value as it presents the experience of a master surgeon for more than 36 years.

R. T. FRANK.

In a foreword to this volume on **Sterility and Impaired Fertility**,<sup>2</sup> Lord Horder stresses the importance of this world-wide problem and refers to the distribution of the etiological factors over many fields of medicine. He suggests that constitutional factors are more important than anatomical factors, and while the problem is one for teamwork, most of the investigation may be done by the family doctor.

In the preparation of this second edition, Lane-Roberts and his co-authors assess the significance and value of much new work in this field, suggest the use and interpretation of postcoital tests, especially the more recent invasion test, the technique of semen analysis, and the determination of pregnandiol in urine. They also add new material in the discussion of cyclical temperature records for the study of ovarian function, and in the use of cytological studies in determining ovarian function.

The opinions expressed in the first edition as to the use of endocrine preparations as therapeutic aids have shown a considerable shift. The use of these hormones is much more precisely defined. The treatment of subclinical infections in the cervix, long recognized as a cause of subfertility, by the sulfonamides and penicillin rather than the cauterization or other surgery is mentioned, and much attention is directed toward constitutional treatment in the elimination of toxic conditions. The use of x-ray stimulation, particularly of the pituitary gland, in the treatment of anovulation is also discussed. The authors bring out the legal, moral, and social aspects of artificial insemination by means of donated semen. While they agree that the short term effects may have been good, and that it has been an acceptable solution to many childless marriages, they caution the possible involvement of dysgenic factors.

The text begins with a general survey of the problems and then treats the male factors in childless marriages in five chapters, comprising 162 pages. Chapter Five, on the male reproductive mechanism and its disturbances, offers technical advice for the urologist or andrologist in addition to much material which should aid the family doctor in his part of the problem.

The two chapters concerning sterility in the female, on the investigation of the woman, and on treatment of the lesions which in her may be responsible for the impairment of her reproductive power are thoroughly considered. The authors, in discussing operations to restore tubal patency, say that the probability that a given operation will result in the restoration of fertility is presumably much lower than some given figures suggest. There is an excellent discussion on tubal insufflation.

There are nine appendices to the text and they bring out the technical details of examination of semen, study for pregnandiol, the biologic tests for pregnancy, and the invasion tests, and the study of waking temperature charts, and the technique, and the dangers, of ovarian and pituitary irradiation. There are many fine photomicrographs and roentgenograms among the illustrations.

<sup>2</sup>**Sterility and Impaired Fertility, Pathogenesis, Investigation and Treatment.** By Cedric Lane-Roberts, C.V.O., M.S., F.R.C.S., F.R.C.O.G., Gynaecological Surgeon, Royal Northern Hospital; Albert Sharman, M.D., Ph.D., M.R.C.O.G., Senior Assistant Surgeon, Royal Samaritan Hospital for Women, Glasgow; Kenneth Walker, M.A., M.B., B.C.(CANTAB), F.R.C.S., F.I.C.S., Jacksonian Prizeman and Hunterian Professor, Royal College of Surgeons, Andrologist, Philip Hill Parenthood Clinic; B. P. Wiesner, D.Sc., Ph.D., F.R.S.E., Consulting Biologist, Royal Northern Hospital; Mary Barton, M.B., B.S., First Assistant to the Fertility Clinic, Royal Free Hospital, London. Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, New York and London, 1948.

The authors are to be congratulated on this new edition which offers an outstanding study of the problem in both partners in a childless marriage, with complete and detailed instruction for investigation, specifically defined indications for treatment, and for the family doctor a good interpretation of laboratory reports, and help in assessing and improving the constitutional problems involved.

PHILIP F. WILLIAMS.

The third edition of Hunt's *Diseases Affecting the Vulva*,<sup>3</sup> appearing within eight years, shows how much appreciated the dermatologic approach has been. Changes have affected therapy mainly. The sulfonamides and penicillin have revolutionized the treatment of venereal disease and are of value in other conditions. Vitamin A is of value in hyperkeratoses; vitamin D in lupus vulgaris; podophyllin in condylomata acuminata. This monograph is of real value and assistance.

R. T. FRANK.

*Gynaecological Histology*<sup>4</sup> by Josephine Barnes consists mainly of 162 microscopic illustrations beautifully reproduced in black and white, with a commentary text. Both normal and abnormal tissues of the female genital tract such as are seen in gynecological practice are described and shown. Purposely, many rare conditions have been omitted as this is designed for the final year of the medical student. Between the short text and the detailed captions, a large amount of ground is covered. There is only one poor illustration, that is Figure 26, of adenomyosis. The classification of ovarian tumors is simple and adequate. The description of carcinoma of both the body of the uterus and of the cervix is very good. The final chapter deals with pregnancy. This is an admirable, simple laboratory guide which is equally good for both student and teacher.

R. T. FRANK.

*Gynecological and Obstetrical Anatomy*<sup>5</sup> by Smout, with chapters on the histology and endocrine control of the female by Jacoby, is in its second edition. In addition to a very detailed osteology with description of the pelvic types, the pelvic joints, the pelvic floor, its connective tissue and fasciae, the uterus, tubes, ovaries, and vagina are described both anatomically and histologically. The hormones and their actions are given in detail. The anatomy of prolapse of the genitourinary tract is described. Chapters on the lymphatics, innervation, the fate of the ovum, the placenta, and the anatomy of the fetus insofar as it affects childbirth are included.

There are 185 illustrations including many colored plates and diagrams illuminating the text which is clear, informative, but dry and somewhat monotonous.

R. T. FRANK.

Two authors, Calle and Restrepo, discuss leucorrhea<sup>6</sup> in three divisions—trichomonas; Donné, casuistic; finally, 700 cases of every variety of leucorrhea including those due to specific organism, presented in a haphazard fashion.

R. T. FRANK.

<sup>3</sup>*Diseases Affecting the Vulva*. By Elizabeth Hunt, B.A., M.D., Ch.B. (Liverpool). Honorary Consulting Dermatologist, South London Hospital for Women; Honorary Dermatologist, New Sussex Hospital for Women and Children, Brighton; Temporarily Honorary Dermatologist, Royal Infirmary, Liverpool; Formerly Senior Medical Officer, Radium Institute and Hospital for Skin and Cancer Diseases, Liverpool; Acting Honorary Dermatologist, Royal Sussex County Hospital, Brighton. Third Edition, Revised. 211 pages. With 36 illustrations and 19 plates in colour. The C. V. Mosby Company, St. Louis. 1948.

<sup>4</sup>*Gynaecological Histology*. By Josephine Barnes, M.A., D.M. (Oxford). M.R.C.P. (London), F.R.C.S. (England), M.R.C.O.G. assistant, Obstetric Unit, University College Hospital, London; Assistant Obstetrician and Gynaecologist, Elizabeth Garrett Anderson Hospital; Surgeon, Marie Curie Hospital. Member Correspondent, Société Française de Gynécologie. With 162 illustrations. 242 pages. Harvey & Blythe, Ltd., London. 1948.

<sup>5</sup>*Gynaecological and Obstetrical Anatomy*. By C. F. V. Smout, M.D., M.R.C.S., Assistant Professor, Department of Anatomy; Sub-Dean and Tutor, Faculty of Medicine, University of Birmingham. With Chapters on The Histology of the Female Reproductive Tract and Its Endocrine Control. By J. Jacoby, M.D., Ph.D., Lecturer in Histology, Department of Anatomy, University College, Cardiff; formerly, Department of Physiology, University of Birmingham. Second Edition. 248 pages, The Williams & Wilkins Company, Baltimore. 1948.

<sup>6</sup>*Flujos Genitales Femeninos*. By Dr. Alonso Restrepo. Trabajos de la Academia de Medicina de Medellín. Reproducción de "Anales de la Academia de Medicina de Medellín". III Época—Vol. III—No. 2—Julio 1946.

### Obstetrics

Twenty-two years have elapsed between the first and the seventh, the present, edition of this book.<sup>7</sup> Certainly it fulfills a useful purpose and must be regarded as having lived up to its title of recent advances. This seventh edition has six new chapters replacing a similar number discarded from the previous edition, and the remainder of the text gives evidence of thorough review of the literature and additions to our knowledge of the two subjects.

The text is characterized by an amplification of the purely physiological details of many of the subjects presented, notably nutrition, weight changes, and water retention in pregnancy, lactation, and hemorrhagic disease of the newborn, and erythroblastosis. The subject of nutrition in pregnancy is amply dealt with and the review of the literature has been critical. The second chapter on weight changes and water retention in pregnancy particularly develops the physiological as well as the pathological influences concerned with this topic. L. J. Davis, of Glasgow, considers anemia of pregnancy under six headings, devoting most of his space to the hypochromic anemias, but giving an excellent discussion of the rarer forms occasionally encountered.

The American literature on caudal anesthesia is reviewed at length. Bourne and Williams feel that it is a method which must be very seriously considered as an addition to our various obstetric analgesics. In a discussion of spinal anesthesia for obstetric surgery, the editors state that it is difficult to avoid the conclusions that this anesthesia is inherently dangerous. The antibiotics are fully discussed in all their applications. The physiological aspects of lactation and recent animal experimentation are given at length to explain the function of lactation in women. Again, in the section on erythroblastosis, the authors devote considerable space to the subject of the Rhesus subgroups and the atypical forms of father, mother, infant reactions.

There are three excellent sections, by Rohan Williams and W. M. Levitt, on radiology in obstetrics, radiological investigation and diagnosis in gynecology, and x-ray therapy in gynecology. The latter two chapters thoroughly supplement an excellent discussion on cancer of the cervix uteri. The physiology and the pathology of the control of urination in the woman is detailed in Chapter Twelve. The anatomico-physiologic mechanism of control is well illustrated and the authors present the technique and illustrations of Aldridge's procedure as well as Millen's sling operation.

The present edition takes stock of the new discoveries and trends in opinion in these two specialties, both as regards the experimental work, and the practical usefulness of new knowledge from the literature of many countries.

PHILIP F. WILLIAMS.

**Midwifery, by Ten Teachers** under the direction of Clifford White and edited by him, Cook, and Gilliatt appears in its eighth edition.<sup>8</sup> The present contributors and editors form an imposing list of British specialists and teachers. The text has been achieved in a unique manner through having one author revise each section in accordance with the reports and suggestions made to him by the other nine contributors. This cooperation and adjustment of opinions and practice give mediated expression of the present teaching of the subject in the British Isles. The textbook is comparable to the larger volumes by American authors; the subject matter is formally presented in forty-seven chapters, thoroughly illustrated.

<sup>7</sup>**Recent Advances in Obstetrics and Gynaecology.** By Aleck W. Bourne, M.A., M.B., B.Ch. (Camb.), F.R.C.S. (Eng.), F.R.C.O.G., Obstetric Surgeon to St. Mary's Hospital; Consulting Obstetric Surgeon, Queen Charlotte's Hospital; and Leslie H. Williams, M.D., M.S. (Lond.), F.R.C.S. (Eng.), F.R.C.O.G., Obstetric Surgeon to In-Patients, St. Mary's Hospital, Consulting Obstetric Surgeon, Queen Charlotte's Hospital. Seventh Edition, 321 pages with 85 illustrations, The Blakiston Company, Philadelphia, Toronto, 1948.

<sup>8</sup>**Midwifery, By Ten Teachers.** Under the direction of Clifford White, M.D., B.S. (Lond.), F.R.C.P. (London), F.R.C.S. (Eng.), F.R.C.O.G., edited by Clifford White, Frank Cook, and William Gilliatt, Eighth Edition, 541 pages with 217 illustrations, The Williams & Wilkins Company, Baltimore, 1948.

It is evident that the advances of the past six years have been well evaluated for inclusion in the revised text. On the whole, one feels that the teaching given here is modern, conservative, and easily understood. The section on management and feeding and injuries and diseases of the newborn comprises one-tenth of the subject matter. It is of interest to note that in the assimilation of the literature and the revision of the text there is no bibliography or reference to specific contribution to the literature.

The conciseness and simplicity of presentation and the jointly considered opinions of ten contributors make the text a valuable contribution.

PHILIP F. WILLIAMS.

Dr. O'Donel Browne's **Manual of Practical Obstetrics**<sup>9</sup> appears in a second edition after a lapse of twelve years, a delay occasioned by the war. This excellent and concisely written manual is intended chiefly for the student and general practitioner and the reviewer feels that the book thoroughly accomplishes the aim of the author. The section on disease of the newborn has been omitted in this volume, but the subject of fetal birth injuries is retained and includes not only specific injuries, but also a short and well-written section on fetal erythroblastosis. The arrangement of the text is logical and the line drawings which are plentiful serve well to amplify the text.

It is apparent that chloroform is still a frequently used anesthetic in labor in England, while the subject of caudal anesthesia is considered in four sentences. A conservative note is struck regarding vaginal operative delivery and it is noted that the illustrations portray application of forceps and delivery in the left lateral as well as the dorsal position. The discussions on puerperal hemorrhage and toxemia show a marked agreement between the practice of the Rotunda Hospital and that of practically any maternity institution in the United States. The classical and the low cervical cesarean sections are well considered; no mention is made of the extraperitoneal technique. The concluding chapter in the book, radiology in obstetrics, by McDonogh, has some well executed roentgenograms. The book is a fine text for students and guide for general practitioners.

PHILIP F. WILLIAMS.

Eden and Holland's **Manual of Obstetrics**<sup>10</sup> has been revised in this ninth edition by Alan Brews. The book has been enlarged by 41 pages, and 40 very excellent x-ray films have been added in addition to over 150 new illustrations. This nearly 800 page book reflects the teachings and practice of obstetrics at the London Hospital and is, therefore, of real interest over here. Every one of the nine parts has been thoroughly revised; particularly, all of the newer improvements in obstetric teaching and therapy which have occurred in the last nine years have been included. Embryology and physiology are given in considerable detail and are very well illustrated. The treatment of hyperemesis and toxemia is about the same as practiced here except that intravenous therapy is not as much emphasized as it might be. In my opinion, curettage for abortion is suggested at too early a stage. The work by American authors on Rh factor, diabetes, toxemia, etc., has been freely and fully incorporated in the text. Rectal examination during active labor deserves more emphasis than it has received. The author agrees that in placenta previa, the modern trend of use of cesarean section is fully justified. While the antibiotics are mentioned and recommended in infection, I find no mention of streptomycin or of the anti-coagulants in the treatment of thrombosis. Obstetric operations are well described and illustrated. The concluding chapter on social care of the patients, which means extra

<sup>9</sup>**A Manual of Practical Obstetrics.** By O'Donel Browne, M.B., M.A.O., M.A., Litt.D., F.R.C.P.I., F.R.C.O.G., Master, Rotunda Hospital, Dublin; King's Professor of Midwifery, Dublin University; Gynaecologist to the Stewart's Hospital, Co. Dublin. Second Edition, 251 pages, with 8 color plates and 218 illustrations, The Williams and Wilkins Co., Baltimore, 1948.

<sup>10</sup>**Eden and Holland's Manual of Obstetrics.** Ninth Edition. By Alan Brews, M.D., M.S. (Lond.), M.R.C.S. (Lond.), F.R.C.S. (Eng.), F.R.C.O.G. Obstetrical and Gynaecological Surgeon, the London Hospital; Director of Obstetric Studies, London Hospital Medical College; Examiner in Midwifery and Diseases of Women, University of Cambridge, the Conjoint Examining Board in England and the Royal College of Obstetricians and Gynaecologists; Late Examiner in Midwifery and Diseases of Women, University of London. With 36 plates, 12 in colour, and 405 illustrations in the text. 796 pages. J. & A. Churchill, Ltd., London, 1948.



rations, maternity benefits, almoner for the care of unmarried pregnant women, applies to the present local conditions in the British Isles.

This is a good book which, with very few changes and additions, would be as popular here as it is abroad.

R. T. FRANK.

A report of the Obstetrical Hospital Cosme Argerich has appeared for 1947.<sup>11</sup> This maternity hospital has from 800 to 1,000 confinements a year. The report contains diverse obstetrical topics by members of the staff. It is a nicely prepared and a very presentable volume.

R. T. FRANK.

**Pregnancy Diagnosis Tests: A Review**<sup>12</sup> by Cowie is an epitome covering the huge bibliography on this subject. As it was published under the auspices of the Commonwealth Agricultural Bureau (Joint Publication No. 13) it deals primarily with veterinary medicine but includes everything on the human being. The author covers seven classes of tests. Among the clinical tests, he mentions the diagnosis in the cow, mare, ewe, goat, sow, and bitch, cat, and rabbit. In the hormonal tests, various animals, mouse, rat, rabbit, guinea pig, male rodents, amphibia, fish, and even plants which are used as indices, are described. Likewise chemical and enzymatic tests are mentioned.

This is a very valuable contribution bringing together under one cover an encyclopedic amount of information. The bibliography is large and universal.

R. T. FRANK.

Discovery of the Rh factor has cast light on erythroblastosis fetalis and some hemolytic reactions following blood transfusion. Under the auspices of the Medical Research Council, Mollison, Mourant, and Race report on the **Rh Blood Groups and Their Clinical Effects**.<sup>13</sup> They deal with the Rh groups, including classification, application to determination of paternity, ethnographic and genetic basis, and calculation of Rh chromosome frequencies. The clinical effects cover production and detection of sensitization, fetal and neonatal effects, premature termination of pregnancy, treatment of the infant by various types of transfusion, etc. In conclusion, Rh testing—typing of cells, tests for Rh antibodies, matching and special tests and techniques—is described. This is a condensed but complete guide.

R. T. FRANK.

Dowkontt, a plastic surgeon, has written a small book on the **Hygiene of the Breasts**<sup>14</sup> designed for the laity. He describes diets for overweight, brassieres for the adolescent, exercises and postures, care during pregnancy. He approves of breast nursing. Diseases, especially cancer and inflammation, are touched upon. Exercises to beautify, hormone creams to develop, operations to reduce, and the corsetière are discussed.

R. T. FRANK.

Lorca's **Textbook on Obstetric Operations**<sup>15</sup> is one of the few Spanish books received by us. It is a large, nearly 700 page, tome with 509 illustrations which, the author emphasizes, are one and all original. They are well executed with lavish use of two colors.

<sup>11</sup>**Anales Del Servicio de Obstetricia del Hospital Cosme Argerich.** Ano 1—Vol. 1. Director Prof. Dr. Juan Leon; Secretario de Radacion Dr. Nino Castelberg. Direccion Hospital Cosme Argerich, Almirante Brown Y Py Margall. 203 pages. Buenos Aires. 1947.

<sup>12</sup>**Pregnancy Diagnosis Tests: A Review.** By Alfred T. Cowie, B.Sc., M.R.C.V.S., Ph.D., National Institute for Research in Dairying, University of Reading. Commonwealth Agricultural Bureaux Joint Publication No. 13. 283 pages Commonwealth Bureaux of Animal Breeding and Genetics, Edinburgh; Dairy Science, Shinfield; Animal Health, Weybridge. Great Britain, 1948.

<sup>13</sup>**The Rh Blood Groups and Their Clinical Effects.** By P. L. Mollison, A. E. Mourant and R. R. Race. Privy Council Medical Research Council Memorandum No. 19. 74 pages. London: His Majesty's Stationery Office, 1948.

<sup>14</sup>**The Hygiene of the Breasts.** By Clifford F. Dowkontt, M.D. 222 pages. Emerson Books, Inc., New York. 1948.

<sup>15</sup>**Tratado Practico de Operaciones Obstetricas.** Por el Dr. Carlos Lorca, De la Cruz Roja Española (Madrid) (Ex Profesor axiliar de Obstetricia y Ginecologia en la Universidad Central; antiguo becario de la Junta Constructores de la Ciudad Universitaria de Madrid; laureado por la Sociedad Ginecologica Española, etc.). Con 509 figuras, totalmente originales, en negro y color. 697 pages. Editorial Científico-Médica, Madrid-Barcelona, Spain. 1948.

Every detail of preparation, instrumentarium, mode of anesthesia, including continuous caudal, intravenous, pudendal, etc., is indicated. The use of the sulfonamides and anticoagulants is described. Penicillin is reserved for the gravest conditions because of its costliness. The Rh factor is discussed.

Among bloodless dilatation methods, the laminaria or tupelo tent still is described. It is used for dilatation in the third and fourth month; in the fifth he packs the cervix or uses bags. Hebostiotomy is described but has little more than historical interest. Version, correction of malposition, and reposition of prolapsed parts are gone into in great detail with ample illustrations. Forty-eight pages are devoted to breech extraction, with 53 illustrations. The fetal mortality is said to be 10 to 20 per cent. Forceps and their use are covered in even greater detail, with 96 illustrations. The mutilating operations are then taken up. The low flap cesarean, the extraperitoneal technique, and the Porro operations are given with indications. In the large clinics of Spain, cesarean operation was performed in from 1 to 5.7 per cent of births.

Repair of birth passages, treatment of exudates, of breast abscesses, and vaginal hysterectomy are described. This volume is very ample and detailed and covers the entire subject minutely. It is unusually well illustrated and faultlessly gotten up.

R. T. FRANK.

**Pathology of Pregnancy** comes from the fluent and prolific pen of Raul Briquet,<sup>16</sup> professor at the University of São Paulo, Brazil. It is an exceptionally well gotten up book with 177 illustrations derived from diverse sources to which due credit is accorded. The chapter bibliographies are right up to date (including 1947) and American sources are widely quoted.

The subject is covered thoroughly: the pregnant woman—infections such as syphilis and tuberculosis, the disturbances of various organs and organ systems including endocrinopathies, dermatoses, malformations, local inflammations of the genital tract, and toxicoses including eclampsia; ovarian pathology—ectopic gestation, placenta previa, abortion, abruptio, hydramnios, mole and chorionepithelioma (where I am pleased to note that Marchand's simple classification is adhered to). The concluding chapter deals with sterility. The book covers the subjects concisely but minutely and adequately and contains an immense amount of information, including methods of treatment.

R. T. FRANK.

Fasc. 8 of *Bibliotheca Gynaecologica*, published by S. Karger, now of Basel and New York contains Merz' **Normal and Pathological Physiology of Lactation**.<sup>17</sup> This 36 page monograph takes up the hormonal secretions which activate the glands, the psychic nervous and physical mechanisms which assist during the lactating phase. Factors leading to difficulties or impediments of lactation are analyzed as well as methods of treatment.

R. T. FRANK.

**Management in Obstetrics** by Claye<sup>18</sup> is designed as an aid for the general practitioner who, though no specialist, is an accoucheur. Abortion, antenatal supervision, diet, vomiting are discussed. Various obstetric conditions, presentations, and complications are dealt with summarily and dogmatically. Except for a few pictures depicting breech extraction, the book lacks adequate illustration. A very elementary and sketchy presentation.

R. T. FRANK.

<sup>16</sup>**Patologia da Gestação.** By Profesor Raul Briquet, Catedrático de Clínica Obstétrica E Puericultura Neo-Natal. Da Faculdade de Medicina Da Universidade De São Paulo. Com 177 Figuras No Texto. 603 pages Editôra Renascença, S.A. São Paulo, Brazil. 1948.

<sup>17</sup>**Normale und Pathologische Physiologie der Lactation.** von W. R. Merz. Aus der Universitätsklinik Basel (Direktor Prof. Dr. Th. Koller). 36 pages. *Bibliotheca Gynaecologica*, Supplementa ad *Gynaecologia*. International Monthly Review of Obstetrics and Gynecology, *Revue Internationale Mensuelle d'obstétrique et de Gynécologie*, *Monatsschrift für Geburtshilfe und Gynäkologie*, Fasc. 8, Redactores E. Anderes-Zürich, Th. Koller-Basel. S. Karger, Basel, Switzerland, 1948.

<sup>18</sup>**Management in Obstetrics.** By Andrew M. Claye, M.D., F.R.C.S., F.R.C.O.G., Professor of Obstetrics and Gynaecology, University of Leeds; Surgeon, Maternity Hospital and Hospital for Women, Leeds; Examiner, Royal College of Obstetricians and Gynaecologists. 186 pages. Geoffrey Cumberlege, Oxford University Press, London. 1948.

Since 1935 Vignes has published a series of monographs on *The Diseases of the Pregnant Woman*. The present brochure entitled *Eclampsie et Eclampsisme*<sup>19</sup> is the seventh. It is a fully documented and exhaustive exposition covering every aspect and containing a minute scrutiny of the world's literature.

R. T. FRANK.

**Reproduction and Survival** by R. Christie Brown<sup>20</sup> postulates that "reproduction aims at the survival and variation of the race but that the individuals participating are mere pawns in the game." Some parents escape lightly, like some of the fishes, others run a hazard but "nature always takes more care of Life than she does of lives." Evolution, selection, survival of the fittest, asexual and sexual reproduction are discussed briefly but clearly. The evolution from the sea, to fresh water, then to the land is marked by the change from careless and simple breeding (oyster, fishes) to complicated reproduction and parenthood.

Primitive reproduction is wasteful. More advanced breeding reduces the number of eggs, increases their size and affords better protection (carried in mouth, in pouch, placenta and uterus). The hormones of reproduction, estrogen and progesterin are described. Along these same lines, evolution, reaction of the embryo to its environment, labor as an instrument of natural selection and allied topics are dealt with. This little book is well worth while and pleasurable reading.

R. T. FRANK.

Volume XXXII of **Contributions to Embryology**<sup>21</sup> contains six articles. Corner (No. 207) discusses alkaline phosphatase in the ovarian follicle and corpus luteum, using six species including the human being. Speert (No. 208) describes the normal and experimental development of the mammary gland of the rhesus monkey. Development, cyclical changes, ablation experiments, pregnancy effects, lactation, etc., were studied. Estrogens, progesterone, androgen and desoxycorticosterone acetate all produced mammary development. Witschi (No. 209) studied the migration of the germ cells of the human embryo from the yolk sac, through the hind gut, mesentery into the mesonephric fold, into the gonadal fold by means of their own active movement. Gillman (No. 210) deals with the development of the gonads in man, the role of the fetal endocrines and the histogenesis of ovarian tumors. Streeter (No. 211) gives a third survey of the "Developmental Horizons in Human Embryos," covering four age groups and their organ development, with amazingly fine detail drawings by Didusch. The final article by Dorcas Padgett describes the development of the cranial arteries in the human embryo.

R. T. FRANK.

### Endocrinology

Turner's **General Endocrinology**,<sup>22</sup> written by a zoologist, is designed less for the medical student, who, however, can obtain much useful information from it, than for the student of biology, the approach being experimental rather than clinical. The author emphasizes that endocrinology should be viewed "as a branch of physiology which deals with the chemical integration of the organism and embraces much more than the conventional ductless glands." Whether, for example, the kidneys should be regarded as an endocrine gland (because of the renin—hypertensinogen-tension mechanism) is a matter of opinion. The "milieu intérieur" and the importance of tissue fluids are emphasized.

<sup>19</sup>**Eclampsie et Eclampsisme.** Par Henri Vignes. 217 pages Maladies Des Femmes Encientes, Masson et Cie, Paris, VI<sup>e</sup>, France. 1948.

<sup>20</sup>**Reproduction and Survival.** By R. Christie Brown, M.D., M.S., F.R.C.S., F.R.C.O.G., Obstetric Surgeon, City of London Maternity Hospital; Hon. Surgeon Samaritan Free Hospital for Women; Gynaecologist, Metropolitan Hospital. 108 pages. Edward Arnold & Co., London. 1948.

<sup>21</sup>**Contributions to Embryology.** Volume XXXII, Nos. 207 to 212. 261 pages. Carnegie Institution of Washington Publication 575, Washington, D. C. 1948.

<sup>22</sup>**General Endocrinology.** By C. Donnell Turner, Ph.D., Associate Professor of Zoology at Northwestern University, Chicago. Illustrated. 604 pages. W. B. Saunders Company, Philadelphia and London. 1948.

Our present techniques do not allow us to differentiate tinctorially the various secretory elements developed by glands. The experimental embryological work on *organizers* and *evocators* in embryologic development, the corticomedullary inductors which determine sex in the bisexual anlage are of fascinating interest as are the phyto hormones of plants.

It is impossible to continue a detailed description of the immense amount of material contained, which covers the usually described internal secretory glands but from a broader viewpoint. In dealing with the pancreas, the gastrointestinal principles are fully described; with the adrenal gland, a very full description of the emergency theory, of the effects on metabolism are taken up. The approach is interesting and in many ways novel. The illustrations are numerous, many of them original delicate line drawings. The book contains a mine of information presented in a fascinating way. Between its covers one finds integrated studies which have appeared in widely scattered departments of research.

R. T. FRANK.

Number 79-80 of the "Spanish Collection of Medical Monographs" is a 68 page brochure by Bishop of London, translated into Spanish by Cañadell on **Gynecological Endocrinology**<sup>23</sup> for the general practitioner.

In addition, there are six shorter articles on diverse topics, four by Spanish authors, one by an English author, and one by an American.

R. T. FRANK.

### Miscellaneous

**Recent Advances in Surgery** by Edwards,<sup>24</sup> with "The Thorax" by Brock, "The Nervous System" by Northfield, and "Radiotherapy in Malignant Disease" by Sir Stanford Cade, is in its third edition. It contains a large amount of accurate and up-to-date information in small compass including all major advances. The American literature is utilized fully.

Information on the electrolyte balance, antibacterial and anticoagulant therapy are included. In addition to thorax and nervous system, the alimentary tract, the blood vessels and the ductless glands are dealt with.

The text is clear and direct, the illustrations numerous, the bibliography adequate. This is an excellent book from which to obtain recent advances quickly and adequately.

R. T. FRANK.

The third edition of Smith and Gault's **Essentials of Pathology**<sup>25</sup> in the same large format with double column of text and 740 illustrations appears after six years. General and systemic pathology with the aim of emphasizing practical and essential factors is featured. Parasitic infestations and cancer, because of their increasing importance, are emphasized. The case histories, 261 in number, roentgenograms and pictures, integrate pathology with clinical subjects, add interest, and give the book a real and broad value rarely attained by the classical books of pathology. The ample and excellent illustrations form a veritable atlas. The short chapter bibliographies are carefully selected. This book is both instructive and interesting.

R. T. FRANK.

<sup>23</sup>**Endocrinología Ginecológica** para el medico general. Por P. M. F. Bishop, D.M. (Oxon.) Profesor de Fisiología aplicada de la Escuela de Medicina del Hospital Guy, Endocrinólogo del Hospital Guy, Endocrinólogo del Hospital de Mujeres de Chelsea. Versión española por el Dr. J. M. Cañadell, Del Departamento de Endocrinología de la Clínica Médica B (Facultad de Medicina de Barcelona). 68 pages. Colección Española de Monografías Médicas. Administración: Ediciones B.Y.P. Barcelona. 1948.

<sup>24</sup>**Recent Advances in Surgery.** By Harold C. Edwards, C.B.E., M.S., F.R.C.S., Surgeon and Lecturer in Surgery, King's College Hospital, London. Surgeon to the Evelina Hospital for Sick Children. Dean of the Medical School, King's College Hospital, Late Consulting Surgeon, Central Mediterranean Forces. Third Edition. With 131 Illustrations. 437 pages. The Blakiston Company, Philadelphia. 1948.

<sup>25</sup>**Essentials of Pathology.** By Lawrence W. Smith, M.D., F.C.A.P., formerly Professor of Pathology, Temple University School of Medicine, Associate Professor of Pathology, Cornell University Medical School, and Assistant Professor of Pathology, Harvard Medical College, Corresponding Member of the Royal Flemish Medical Academy of Belgium; and Edwin S. Gault, M.D., F.C.A.P., Associate Professor of Pathology and Bacteriology, Temple University School of Medicine. With a foreword by the late James Ewing, M.D., Memorial Hospital, New York City. Third Edition. 764 pages. The Blakiston Company, Philadelphia and Toronto. 1948.



In this book, **The Mechanism of Abdominal Pain**, Dr. Kinsella<sup>26</sup> suggests that mechanism for splanchnic pain does not differ essentially from that for somatic pain. He states that the underlying factors, anatomic and physiologic, are identical as are also the effective painful stimuli, whether physical (experiment) or pathological. After briefly reviewing the various conceptions of abdominal pain, the text proceeds to describe in detail the three pathways, bulbar, thoracolumbar, and sacral, which carry the nerve impulses from the abdominal viscera to the central nervous system.

Various succeeding chapters take up visceral sense, referred pain, cutaneous reactions, tenderness and rigidity, adhesions, and the various sections of the alimentary tract. In Chapter fifteen the author refers to the pain of appendicitis as having two components, the visceral and the parietal, and the origin and pathways of these impulses are discussed, repeating to a certain degree the previous analysis (Chapter Six) of cutaneous hyperalgesia in appendicitis. He notes the atypical distribution of pain in the normally placed appendix as well as in the abnormally situated organ, and refers to the importance of the psoas ridge in promoting the remarkable constancy of McBurney's point.

He raises three points of interest regarding pain arising in the uterus and adnexa: the persistence of pain during labor following presacral neurectomy; again, the pain produced by palpation of an inflamed ovary in the pouch of Douglass, especially when overlain by a retroverted uterus. He considers this an expression of direct visceral tenderness since parietal peritoneum does not lie between the affected viscus and the examining finger; and finally, that the pain produced on grasping an inflamed cervix with a vulsellum proves that the apparent insensitivity of the viscera is only relative; that visceral pain may arise not only direct by disordered motor activity, but also through inflammation. In the final chapter he sums up his reasons for belief in direct visceral tenderness as well as for direct visceral pain, concisely summarizing his theories and the proofs as he has found them.

PHILIP F. WILLIAMS.

The aim of the book, **Physiologic Therapy in Respiratory Diseases**, by Dr. Barach,<sup>27</sup> as in an earlier text by him on inhalation therapy, is to bring out the principles and practices of physiologic therapy in respiratory disease. The therapeutic use of gas and other measures which have a specific value in counteracting clinical disorders of breathing are discussed. The pathologic physiology of each clinical entity is explained, as well as the physiologically based procedures by which it may be combated. The subject of practical techniques in current use has been thoroughly considered. After a short section on the historical background of the topic, there is an extended presentation on anoxia. This is followed by a concise chapter on each of the various etiologic lesions and their therapy.

Of interest to gynecologists and obstetricians should be the chapters on massive collapse of the lungs and postoperative atelectasis. Seventy per cent of the former follow surgical operation and injury. The treatment recommended is inhalation of from 5 to 7 per cent carbon dioxide and oxygen to stretch the bronchial walls by maximum expansion of the chest in hope of freeing the usual mucous plug, and having it subsequently coughed up. Inhalation of from 50 to 70 per cent oxygen is regarded as useful as generally indicated in the maintenance of respiratory function before and after the carbon dioxide therapy. The author discusses the effect of anesthetic agents and the reduction of vital capacity by the abdomen in producing postoperative atelectasis. The preoperative use of penicillin and hyperventilation is mentioned as well as bronchoscopy, intubation, and aspiration.

<sup>26</sup>**The Mechanism of Abdominal Pain.** By V. J. Kinsella, M.B., Ch.M. (Syd.), F.R.C.S. (Eng.), F.R.A.C.S., Hon. Surgeon, St. Vincent's Hospital, Sydney, Hon. Surgeon, Hornsby Hospital. 210 pages and 17 illustrations, Australasian Medical Publishing Company Limited, Sydney, 1948.

<sup>27</sup>**Physiologic Therapy in Respiratory Diseases**, by Alvan L. Barach, M.D., Associate Professor of Clinical Medicine, Columbia College of Physicians and Surgeons; Assistant Attending Physician, Presbyterian Hospital New York, N. Y. Second Edition. 396 pages with 74 illustrations. J. B. Lippincott Company, Philadelphia, London, Montreal, 1948.

In discussing asphyxia of the newborn, both antenatal and postnatal, the author refers to the large part this plays in the mortality of the newborn on the first day of life. The causes of asphyxia before delivery are enumerated, and the influence of anesthetic and analgesic agents is stressed. The disturbances of the placental circulation are mentioned, and stress is laid on the importance of recognition of intrauterine anoxia, pointing out the significance of both sudden drops and persistent slowing of the fetal heart beat. He suggests the therapeutic use under these circumstances during labor of oxygen administration to the mother.

The pathology of asphyxia is well described and the author discusses mouth-to-mouth insufflation, inhalation of 5 per cent carbon dioxide and oxygen, and the use of pure oxygen. Infants who finally breathe with any measure are best protected by incubation and 50 per cent oxygen atmosphere for some time after birth. The value of drug treatment of apnea is questioned. The author discusses the mechanics used for resuscitation.

The methods of physiologic therapy, including the apparatus for inhalation therapy, the use of pressure and administration of aerosols, is thoroughly gone into, and the techniques of many types of instruments fully explained. While the volume will be particularly interesting to those dealing with acute and chronic respiratory disease, it should also be of great help to divisions of anesthesiology which today in many hospitals are intimately concerned in the administration of these methods of physiologic therapy.

PHILIP F. WILLIAMS.

The three-volume **Clinical Laboratory Methods and Diagnosis**<sup>28</sup> in its fourth edition is an increasingly ambitious attempt to cover all phases of laboratory technique with concise interpretations. It succeeds fairly well in 3,103 pages. The good handiwork of co-authors improves particularly the partially revised sections on bacteriology, protein metabolism and parenteral protein hydrolysate therapy, toxicology and police crime methods, optical crystallography, parasitology and tropical medicine, Rh factor, antibiotics and their assay, and electrocardiography.

Up-to-date laboratory information is presented relative to antibiotics, salmonella organisms, virus diseases in general, atypical pneumonia, influenza, vaginal smears, and toxicologic problems. Improvement in procedures such as "blood-phenol level" and "protein-bound iodine," although not as yet universally used, should have been noted.

A very useful portion of the material is an accurate compilation of techniques selected from personal experience, personal communications, and from the literature. Unfortunately, a good many of the techniques, terms, and references to the literature are principally of only historic interest. Further, there is an unfortunate introduction of commercialism by the tendency to show undue preference for equipment and reagents of certain manufacturers, instead of naming several or all interested firms.

The subject matter is well organized and clearly presented. Many intricate facts and theories are simply and logically explained to furnish an easy and adequate working knowledge for the uninitiated. However, the author lapses into the history of an isolated case all too frequently to illustrate a point. Of note are certain ambiguous statements, e.g., the inaccurate suggestion that splenectomy is ordinarily useful in leucemia. Nevertheless, there are many minute pearls (such as "short cuts" in technique) available to a semi-experienced and wary physician or technologist. One attraction to this set of books is the fact that there is nearly always available a procedure which yields an answer useful to the clinician.

Most illustrations are good, e.g., vaginal and bronchial smears, smears of nasal secretion, and the pictures of colorimetric reactions. The hematologic color plates are fair. Many of the old illustrations are poor and their legends do not state the degree of magnification. The index is well organized and complete.

<sup>28</sup>**Clinical Laboratory Methods and Diagnosis.** By R. B. H. Gradwohl, M.D., D.Sc., F.R.S.T.M. and H. (London), Director of the Gradwohl Laboratories and Gradwohl School of Laboratory Technique; Pathologist to Christian Hospital; Director, Research Laboratory, St. Louis Metropolitan Police Department, St. Louis, Missouri. Fourth Edition. Volumes I and II, 2284 pages, with 691 illustrations and 51 plates. Volume III, separately indexed, 819 pages, with 420 illustrations and 7 plates. The C. V. Mosby Company, St. Louis, 1948.

Volumes I and II may be purchased as a unit and are most useful to the laboratory of the small hospital where economy is necessary and where experts in the subdivisions of the laboratory are not available. Volume III is a very well illustrated, fairly complete treatise on parasitology and tropical medicine which may be purchased separately, if desired. It is written with the coauthorship of Dr. Pedro Kouri, Director of the Institute of Tropical Medicine and Professor of Parasitology and Tropical Medicine in Havana University.

PHILIP F. WILLIAMS.

The second **Index Volume of Surgery, Gynecology & Obstetrics**,<sup>29</sup> recently issued, constitutes a valuable and comprehensive presentation for ready reference of the contents of this important periodical publication for a period of twenty years from July, 1925, to July, 1945. The wealth of material contained in its 750 pages, effectively indexed and cross indexed, provides an adequate bibliographic survey of these fields of medicine. The book is recommended as an admirable work of reference.

GEO. W. KOSMAK.

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## Item

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### Fellowship Announcement

A Fellowship in obstetric and gynecologic endocrinology will be available at the Jefferson Medical College and Hospital on or about May 1, 1949, under the direction of Dr. A. E. Rakoff, Assistant Professor of Obstetrics and Gynecology, and Endocrinologist to the Department of Clinical Laboratories.

The Fellowship is available to Doctors of Medicine who have had at least one year or its equivalent of postgraduate training in obstetrics and gynecology. Applicants for the Fellowship should communicate at once with Dr. Lewis C. Scheffey, Professor of Obstetrics and Gynecology, Head of Department, and Director of Division of Gynecology, Jefferson Medical College and Hospital, Philadelphia 7, Pa.

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<sup>29</sup>**Index, Surgery, Gynecology & Obstetrics**, Volumes 41-80, 1925-1945. Editor, Loyal Davis, Associate Editors, Sumner L. Koch, Michael L. Mason, Assistant Editor, M. E. Spencer. Published by the Franklin H. Martin Memorial Foundation, 24 East Erie Street, Chicago, Illinois.

## Correspondence

### Irradiation in the Treatment of Amenorrhea and Sterility

*To the Editor:*

When irradiation was suggested for the treatment of amenorrhea and sterility many years ago, it met with a great deal of adverse criticism because of the supposed possibility of injury to the children born of irradiated mothers. This criticism continued with increased furor up to the present time when the effects on animals were utilized to prognosticate the abnormal effects that might be expected in human beings following irradiation of their reproductive organs.

In 1928, I reported in the *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY* my first series of cases treated by x-ray therapy and stated, "When properly treated no harm ensues to the patient or to her offspring." Since that time, over the course of twenty-five years, I have treated several hundred women for sterility, with the birth of more than 150 children perfectly normal in every way. Several reports of this work have been published from time to time.

However, what of the children of these children born of irradiated mothers? No one as yet had reported on this third generation. Again, based only on animal observations, dire calamities were predicted for the children of those born of irradiated mothers.

I warned against accepting this prognostication, but of course had to wait until the children of irradiated mothers matured and married and reproduced. I am now ready to report on a third generation baby. This baby boy was born on Oct. 25, 1948, to a young woman who was born to an irradiated mother in January, 1927. This baby boy is entirely normal and is the first third generation child born of irradiated mothers.

The history in this case is as follows:

Mrs. H. A. was referred to me, by Dr. I. C. Rubin, on June 9, 1925, for amenorrhea, dysmenorrhea, and sterility. She was 28 years of age. Menstruation began at 11 and was never regular. She married at 26 and continued to have irregular, painful periods and had not been able to conceive. Her last period was on May 3, 1925.

She received a course of x-ray therapy to the ovaries in the prescribed manner between June 9 and June 30, 1925. Following treatment, the patient menstruated regularly for nine months without pain, became pregnant, and in January, 1927, gave birth to a normal baby girl.

This baby girl matured normally, menstruated regularly beginning at the age of 13. She was married on March 4, 1946. Contraceptives were used until last year. She became pregnant and now, on Oct. 25, 1948, gave birth to a perfectly normal baby boy, weighing 6 pounds at birth.

I feel warranted, therefore, in reiterating my previously published conclusions that irradiation, when properly given, is harmful neither to the mother nor to the offspring and that it has proved a valuable therapeutic procedure for the treatment of amenorrhea and the relief of sterility.

Because my original report was published in this *JOURNAL* and because I should like to bring this successful conclusion to the attention of the profession so that they may now employ this method in the treatment of sterility without fear of abnormal consequences, this letter brings the data on this subject up to date.

IRA I. KAPLAN, M.D.

755 PARK AVENUE,  
NEW YORK.  
Oct. 30, 1948.



## Items

### **International and Fourth American Congress on Obstetrics and Gynecology** **May 14 to 19, 1950, Hotel Statler, New York City**

Further plans for holding this international gathering have recently been announced by the sponsoring group, the American Committee on Maternal Welfare.

The preliminary program for the scientific sessions, as developed by the General Program Committee of which Dr. Howard C. Taylor, Jr., of New York is the chairman, is as follows: The morning meetings, Monday through Friday, May 15 to 19, are general sessions each devoted to one of five topics, (1) physiology of human reproduction, (2) the pathology of human reproduction, (3) social and economic problems, (4) neoplastic diseases of the female reproductive system, and (5) obstetric and gynecologic procedures.

The afternoons will be given over to meetings of various groups represented at the Congress, including nurses, nurse-midwives, hospital administrators, educators, practicing physicians, investigators in special fields, and public health doctors and nurses. Arrangements for these meetings are under the direction of the following committees: medical section, Dr. Newell W. Philpott, Montreal, Quebec; educators and investigators, Dr. George W. Corner, Baltimore, Maryland; hospital administrators, Dr. G. Otis Whitecotton, Oakland, California; public health, Dr. Edwin F. Daily, Washington, D. C.; and nurses and nurse-midwives, Miss Margaret A. Losty, R.N., of New York City.

The technical exhibit is under the direction of a special committee of which Dr. Woodard D. Beacham of New Orleans is chairman. Dr. John Parks of Washington, D. C., heads the committee in charge of the scientific exhibit. The committee in charge of arranging the motion picture program is under the direction of Dr. Archibald D. Campbell of Montreal. Applications for space in the scientific exhibit or for time on the motion picture program should be submitted to the chairmen in charge of these activities on official application blanks obtainable from the business office of the International Congress at 24 West Ohio Street, Chicago 10, Illinois.

All inquiries pertaining to the meeting should be addressed to the Chairman of the International and Fourth American Congress on Obstetrics and Gynecology, Dr. Fred L. Adair, at 24 West Ohio Street, Chicago 10, Illinois.

### **The Twelfth British Congress of Obstetrics and Gynaecology** **July 6, 7, 8, 1949, London, England**

#### **Program of Proceedings**

**WEDNESDAY, JULY 6, 1949.**

*Morning Session.* 10 A.M. Chairman: The President, Sir Eardley Holland.

The Congress will be declared open by the Minister of Health.

#### **"Modern Caesarean Section"**

Introduced by Mr. C. McIntosh Marshall (Liverpool).

Openers of Discussion:

1. Mr. A. W. Purdie (London).
2. Dr. Bécélère (Paris).

Invited Speakers:

1. Dr. Ninian Falkiner (Dublin).
2. Mr. Frank Stabler (Newcastle).

*Afternoon Session.* 2 P.M. Chairman: Professor Hilda Lloyd.

- (1) Guest Paper, "Endometriosis," Dr. Joe Meigs (Boston, Mass.).
- (2) "The Methods of Assay and Clinical Significance of Pregnanediol in the Urine."

Introduced by:

1. Professor C. F. Marrian (Edinburgh).
2. Dr. G. I. M. Swyer (London).

## Openers of Discussion:

1. Dr. F. S. Parkes (London).
2. Dr. S. Bender (Liverpool).

## Invited Speakers:

1. Dr. P. M. F. Bishop (London).
2. Dr. C. Crooke (Birmingham).

8:45 P.M. Reception by the President and Council of the Royal College of Obstetricians and Gynaecologists at the University of London, Bloomsbury, W.C.1.

## THURSDAY, JULY 7, 1949.

*Morning Session.* 10 A.M. Chairman: Sir William Gilliatt.

## "Essential Hypertension in Pregnancy"

## Introduced by:

1. Professor George W. Pickering (London).
2. Professor F. J. Browne (London).

## Openers of Discussion:

1. Mr. G. F. Gibberd (London).
2. Mr. A. Dickson Wright (London).

Invited Speaker: Professor R. J. Kellar (Edinburgh).

*Afternoon Session.* 2 P.M. Chairman: Dr. John Hewitt.

- (1) "The Management of Pregnancy in Diabetics."

## Introduced by:

1. Mr. John H. Peel (London).
2. Dr. G. Douglas Matthew (Edinburgh).

## Opener of Discussion:

1. Dr. W. G. Oakley (London).
- (2) "Hernia of Pouch of Douglas."

Introduced by: Mr. Charles D. Read (London).

## Openers of Discussion:

1. Mr. A. A. Gemmell (Liverpool).
2. Mr. Alexander C. Palmer (London).

## Invited Speaker:

1. Mr. C. M. Gwillim (London).

8-10:30 P.M. Reception by the President of the Congress at the Zoological Gardens by courtesy of the Council of the Zoological Society of London.

## FRIDAY, JULY 8, 1949.

*Morning Session.* 10 A.M. Chairman: Professor O'Donel T. D. Browne.

## "Modern Concepts in Diagnosis, Treatment and Prognosis of Carcinoma of the Uterus."

- (1) "The Diagnosis by Vaginal Smear." Dr. J. E. Ayre (Montreal).
- (2) "Precancerous Cellular Changes in Carcinoma of the Cervix." Professor Gilbert I. Strachan (Cardiff).
- (3) "Prognosis Based on Biopsies." Mr. A. Glucksmann (Cambridge).
- (4) "The Operation of Pelvic Exenteration." Dr. Joe Meigs (Boston, Mass.).

A discussion will follow each paper.

*Afternoon Session.* 2 P.M. Chairman: Dr. E. Chalmers Fahmy.

## Discussion on Maternal Mortality.

Introduced by: Sir William Gilliatt.

## Openers of Discussion:

1. Professor Dugald Baird (Aberdeen).
2. Mr. Percy Stocks (Leeds).
3. Sir Eardley Holland (London).

## Invited Speakers:

1. Dr. G. W. Theobald (Leeds).
2. Dr. H. R. MacLennan (Glasgow).

7:45 P.M. Congress Banquet in Guildhall.

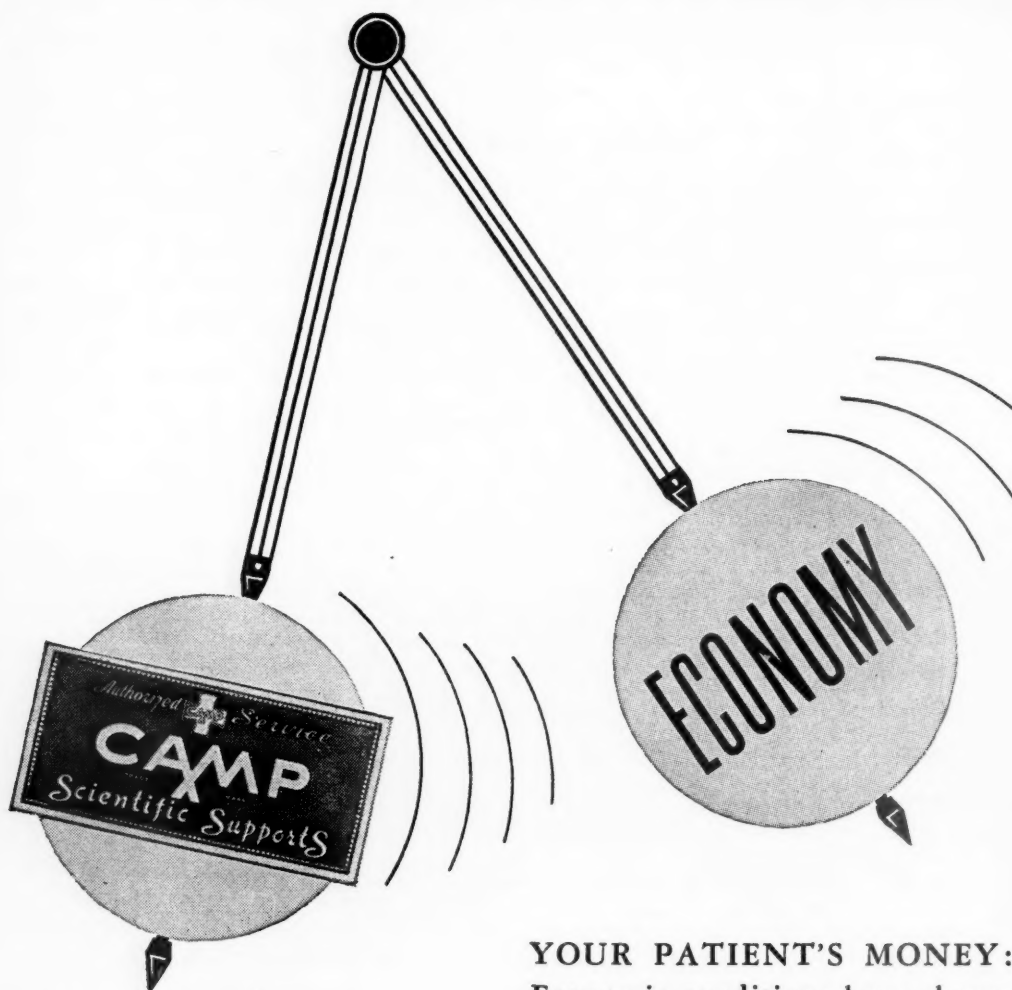
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# American Journal of Obstetrics and Gynecology

**Editor: GEORGE W. KOSMAK**

**Associate Editors: HOWARD C. TAYLOR, JR., and WILLIAM J. DIECKMANN**

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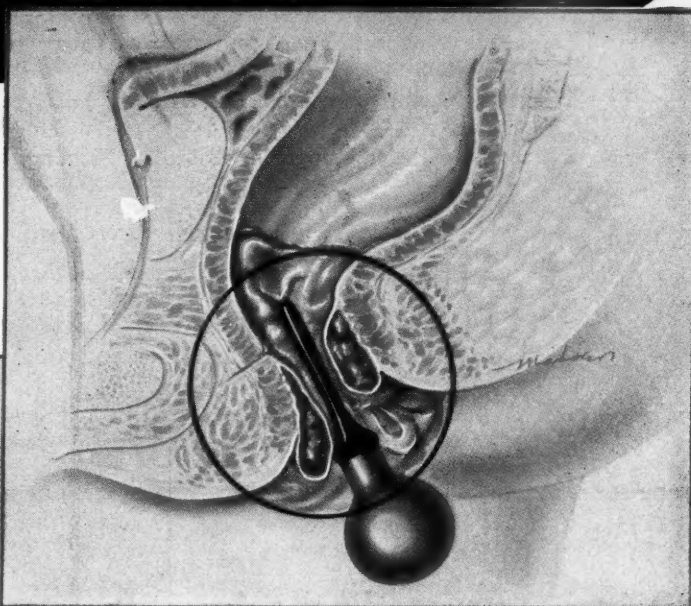
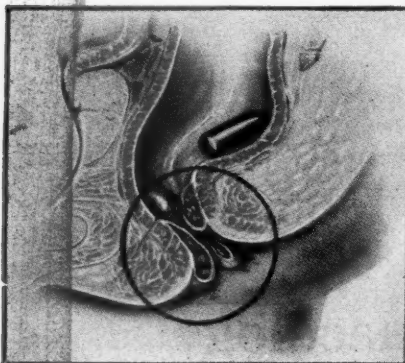
<b>Fred L. Adair</b> <b>Brooke M. Anspach</b> <b>James R. Bloss</b> <b>Lucius E. Burch</b> <b>Walter W. Chipman</b> <b>Willard R. Cooke</b> <b>Harry S. Crossen</b> <b>Thomas S. Cullen</b> <b>Arthur H. Curtis</b> <b>William C. Danforth</b> <b>Walter T. Dannreuther</b>	<b>Carl H. Davis</b> <b>Robert L. Dickinson</b> <b>Palmer Findley</b> <b>C. Frederic Fluhmann</b> <b>Robert T. Frank</b> <b>William P. Healy</b> <b>F. C. Irving</b> <b>James C. Masson</b> <b>Harvey B. Matthews</b> <b>James R. McCord</b> <b>Norman F. Miller</b>	<b>Emil Novak</b> <b>Everett D. Plass</b> <b>Isidor C. Rubin</b> <b>Otto H. Schwarz</b> <b>Paul Titus</b> <b>Herbert F. Traut</b> <b>Norris W. Vaux</b> <b>George Gray Ward</b> <b>Benjamin P. Watson</b> <b>Philip F. Williams</b> <b>Karl M. Wilson</b>
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## RECTALGAN

**provides immediate Symptomatic Relief on application following PERINEAL SUTURING in Obstetrics and Gynecology**

**Also in HEMORRHOIDS and PRURITUS**

**NOT A SUPPOSITORY  
NOT AN OINTMENT**



With RECTALGAN there is no waiting time for the vehicle to melt or dissolve while at rest in the ampulla.

### FORMULA:

Benzocaine .....	4.5	%
Carbolic acid .....	1.75	%
Menthol .....	0.5	%
Ephedrine Alk .....	0.125	%

DISSOLVED IN OILS Q. S.  
(MALLON PROCESS)

**SUPPLIED:** In bottles of 55 cc. (approx. 24 applications) with self-lubricating Rectal Applicator.

**AVAILABLE:** At all pharmacies.

### RECTALGAN — The Liquid Topical Anesthesia in HEMORRHOIDS and PRURITUS

when applied, spreads and covers the entire involved pathologic area. It is absorbed rapidly . . . being non-occlusive will penetrate even the minutest fissure . . . and its efficient anesthetic and anti-pruritic action is noted almost immediately. Its simplicity of use and freedom from distasteful features are greatly appreciated by the fastidious patient.

Strictly an ethical product advertised only to the profession.

*Trial supply sent to physicians on request.*

**MALLON DIVISION of DOHO CHEMICAL CORP., New York 13, N. Y. • Makers of AURALGAN and O-TOS-MO-SAN**